cases. The question depends on finding out whether such irritants are, in general, favorable to cancer formation or whether tar derivatives play a leading role in this respect, and finally, whether they are of special significance in the origin of carcinoma of the bronchi. Naturally, that must be though of, since the air passages are particularly exposed by inhalation to many street-borne irritants. Experimental work was done by Brandt, but he could observe only a resulting effort toward regeneration, early signs of malignant growth of the basal cells and bronchial mucous membrane, and not a clearly defined indisputable cancer.'

It is the importance of tar in the experimental genesis of lung cancer that necessitates its consideration here. Möller (2423) painted the backs of young rats with it and obtained the cornified squamous epithelial variety of lung carcinoma in all animals that survived 300 days of painting. He considered two possibilities - that the carcinogenic particles could have traveled either by the blood stream or by inspired air - and then he mentioned hematologic origin of the bladder cancer of aniline dye workers. To a certain extent the work of Murphy and Sturm (2520) corroborates Möller's results (2423), yet the conclusions drawn differ. The former painted the skin of white mice over ever-changing areas for a long time, and thus in two series produced approximately 60-78 per cent, respectively, of multiple epithelial tumors. These tumors were exactly similar to the spontaneous cancer of the lungs of mice which had been characterized by different authors as adenocarcinoma, papillary cystadenoma and adenoma. These authors did not believe that the tumor was transmitted from the skin or that it was caused by tar licked in and resorbed through the intestines but that the application of tar to the skin lowered the resistance to carcinoma and the subsequent inhalation of foreign irritating substances such as hay dust or saw dust led to carcinomatous, cellular proliferation. Febiger, Kennaway, Dreyfuss and Bloch obtained lung cancers by painting white mice for a long time with tar fractions. Kimura (2321) was able to produce pulmonary cancer in one rabbit and three guinea-pigs through insufflation of tar through a tracheo- tomy tube. The case of von Meyenburg is clinically interesting in this connection. The patients, a hairdresser, developed pulmonary cancer after having been engaged for some time in the manufacture of tar soap. These facts point attention to a possible relationship between street-tarring and lung cancers.

Jamagiva said that the increase in lung neoplasms may be attributable to tar dust of roads and streets. Heilmann (2528) referred to the possible dependence of bronchial cancers on the effects of particles of tar, oil and other substances raised by automobile traffic. Bloch's work with Dreyfuss showed that fine dust particles found with varying frequency in different tars must be kept in mind in this connection; the former of these authors, addressing the Swiss street workers' union in 1924, emphasized tarring of streets as a cause of cancer of the lungs. Goltz

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(3030) contrasted the annual use of half a million tons of tar on the roads of the United States with the fact that in Hong Kong none of it is used and cancer of the lung is a rarity. Simpson (2927), too, regarded the rarity of lung cancer in Hong Kong and in Singapore, where also no tar is used, as suggestive, for, he said, both clinically and experimentally it is known that tar is a potentially carcinogenic substance.

To refute these suggestions, Konrad and Franke (2955) denied that the increase of the disease in Riga is due to either an increased number of automobiles or an increased use of tar, since neither of these increases has taken place. Probst (2732) concluded, from data furnished by the engineer for the canton of Zurich and the street inspector of the city of Zurich, that road tar exercised no influence on the incidence of pulmonary new growths. Husted and Biilman (3724) were unable to demonstrate relationship between the frequency of pulmonary carcinoma in Denmark and the more extensive tarring of roads. Jaffe (3516) recently pointed out that pulmonary cancer is very common in countries where road tarring is little used, as, for example, in Russia. No evidence could be found by the Kennaways that tarring of the roads has affected the incidence of pulmonary carcinoma in the general population. Such data as are available suggest that coal tar in the atmosphere, whether derived from roads or from any other source, does not readily cause cancer of the lung. Furthermore, an investigator who has exposed mice to an atmosphere highly contaminated with road dust containing two per cent of tar found no pulmonary carcinoma among his animals, even though malignant tumors did arise in the skin.

Also in Basel, Staehelin (2526) found that increased frequency of lung cancers was disproportionate to increased tarring of streets. There, street-tarring was started in 1903, lapsed until 1906, when it was increased so that now 42.2 per cent of the street area is tarred. The increase of pulmonary cancers in 1912 might be explained as due to this cause, but were this the case there should have been a noticeable increase since the War; this has not developed. Staehelin further pointed out that the disease did not start to increase in France directly after 1880, when tarring started there, and that though the practice has continued to the present, Ribadeau-Dumas in 1923 mentioned only two to four lung cancers per 1,000 sections in that country. Vincent made a survey which disclosed no positive relation between the disease and the prevalence of street-tarring in France. So Staehelin argued that it is easier to demonstrate a causal relationship between cancer in general and street tar dust than between the latter and bronchiogenic cancer in particular.

It seems sensible to conclude that inhalation of particles of tar taken into the air from streets and roads may be counted among the chronic irritants responsible for pulmonary carcinomas but that it is in no sense their sine qua non cause." (pages 79-82 of ref. 3702)

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Presently, it is no longer necessary to measure tar particles directly, but to collect the benzopyrene component. In more comprehensive studies, hydrocarbons and polycyclic aromatic amines are analyzed in detail. The ozone level used as primary pollutant indicators for enforcing provisions of Clean Air Act represent the end results of vehicular emissions and prevailing wind velocity (Part Four).

Occupational Exposure.

Prior to the 1930's, there was significant number of publications on tar skin cancer, both human studies and animal experiments. The human studies on lung cancer associated with fossil fuel products and combustion emission consisted of reviewing occupational history. Duguid (2721) observed that outdoor workers were more represented than indoor workers in a group of 143 lung cancer patients compared to the general population of Manchester. Harris covered the subject of occupational exposure by the following SOA statement:

> "5.3. Beginning in the 1920s, a variety of factors were hypothesized as contributing to the striking rise in lung cancer. These included: the influenza pandemic of 1918; old tuberculous lesions in lung cancer patients; pre-existing bronchitis and emphysema in lung cancer victims; gasoline fumes containing lead; diesel and gasoline-powered automobile emissions; irritant gases used in World War I warfare; soots, tars and other air pollutants from roads, fuel combustion, and various industrial processes; as well as the rise in cigarette smoking. A concentration of lung cancer cases in the mining district of Schneeberg in Saxony stimulated interest in radioactive substances and certain heavy metals as possible contributors. (See Perret 1929; Hoffman 1929, 1931; Ochsner and DeBakey 1941; Kennaway and Kennaway 1936, 1941)"

It should be noted that Harris did not mention Duguid and the almost fifty articles discussed in the next paragraphs and tables. Kennaway and Kennaway

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appeared in the above list of references and the discussions starts with this couple.

Lung cancer deaths in England and Wales. Kennaway and Kennaway examined 18,280 death certificates for lung cancer in males from England and Wales from 1921 to 1932 inclusive. A group of open-air occupations, where there was exposure to dust of roads, had rather high ratios for cancer of the lung. Workers exposed to coal gas and tar, and those engaged in preparation and sale of tobacco, tend to show an increased prevalence of cancer of the lung. The observation on tobacco manufacturers has been transposed by some in support of concept that tobacco smoking was a causative factor of lung cancer (3632). Kennaway & Kennaway discussed the quesion whether tarring of roads contributed to increase in lung cancer deaths. The first of seven numbered paragraphs was on the positive results of animal experiments that are discussed under the next subtopic. The remaining six paragraphs were as follows:

> "(2) In spite of the rather high incidence of lung cancer in those occupations where there is exposure to road dust, it seems wholly unreasonable to attribute the recent increase of this disease among the general population to the tarring of roads. For scores of years before this increase began coal tar was being discharged into the atmosphere in the form of soot by the domestic fire in quantities vastly greater than any which could now be derived from the roads. Tarring of roads must undoubtedly increase the amount of dust derived from tar in the air, but this increase appears negligible in comparison with the amount of soot present already. One sees clouds of smoke drifting over any large town, but one does not see any similar clouds of tar-laden vapour arising continually from tarred roads.
>
> (3) The contamination of the air with soot has probably been decreasing, owing to the greater use of gas and electricity, before and during the period when the recorded cases of cancer of the lung have been increasing rapidly.
>
> (4) Moreover, such evidence as is available suggests that coal tar in the atmosphere, whether derived from roads, domestic chimneys, or any other source, does not readily give rise to cancer of the lung. Chimney sweeps, who of all persons are most exposed to soot, have not a very high ratio for lung cancer, and the other

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occupations where there is special exposure to the products of the gas-works (gas stokers, gas works foremen and inspectors, gas fitters, Table IX) show an incidence of lung cancer which is from two to four times that prevailing in the general population. This increased liability, though very undersirable, cannot be regarded as a very high industrial risk. It does not even approach, for instance, the increase of risk of fatal cancer of the scrotum which is incurred in the occupations of chimney sweep or mule-spinner.

(5) Cancer of the lung can undoubtedly be produced by an external agent, for the Schneeberg miners show an extremely high incidence. (Out of 154 miners twenty-one died in 3-1/2 years, and cancer of the lung was found in every one of thirteen of these submitted to autopsy, while of the eight not examined post mortem two had given in life strong evidence of the presence of this disease (Rostoski, Saupe and Schmorl, 1926). These remarkable data make all the more distinct the indication that the potency of coal tar products, though seen clearly in occupations where there is abundant exposure to these, is nevertheless of a low order. Corroborative evidence of this low potency is afforded by the case of the mule spinners who show an especially small liability to cancer of the lung although they inhale air sprayed with an oil which produces cancer of the skin.

(6) Two phenomena which might be discussed in relation to the tarring of roads and cancer of the lung are (a) the parallel increase in lung cancer in country dwellers and town dwellers and (b) the greater increase in lung cancer in men than in women. But one can always argue that tarred roaads do, or do not, now penetrate to all parts of the country, or that women, are, or are not, exposed as much as men to road dust, so no useful purpose would be served by any such discussion.

(7) The similarity has been noticed between the curves showing (a) the recent increase in cases of cancer of the lung and (b) the onset of mule-spinner's cancer (of the skin) after 20-25 years' employment in cotton mule spinning (Henry, (2824)), and the suggestion might be made that the sudden increase in cases of cancer of the lung was traceable to the introduction of tarring of roads about 20 years earlier. But, even if one suppose that road dust is active in producing cancer of the lung, it is wholly improbable that the exposure of the general population to this dust is comparable to the intensive exposure to oil which occurs in the mule room." (page 263-265 of ref. 3632)

Although the Kennaways were critical of the role of tarring of roads, their comments were not applicable to other form of coal tar of which there were at least six entities. Kennaway and his colleague reported on chemical and

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biologic effects of tar and their overall conclusion was that polycyclic aromatic hydrocarbons caused lung cancer in mice (see below, under European Research on Experimental Carcinogenesis).

Tabulated results and opinions on occupational and environmental factors. The literature of the 1930's can be grouped to the following categories: Group (a) Health hazards of occupational/environmental factors with no mention of tobacco smoking (11 publications); Group (b) Health hazards of occupational/environmental factors with tobacco smoking mentioned and no indications of preferential cause (6 publications); Group (c) Question health hazards of occupational/environmental factors with no mention of tobacco smoking (9 publications); Group (d) Question health hazards of occupational/environmental factors with mention of tobacco smoking (8 publications). The grouping is based on whether the authors favored, questioned, or simply mentioned, occupational/environmental factors separately from tobacco smoking.

Group (a) Health hazards of occupational/environmental factors with no mention of tobacco smoking.

Authors Geographic Location	Results and Comments
(3019) Miller & Jones New York	There were 32 case reports, more than half, laborers exposed to dust, paint and combustion emissions. "From this brief review it is evident that we have a considerable number of theories as to the causation of pulmonary carcinoma which have very little basis of proved fact. We are inclined to agree with authors such as Katz (2731) that the metaplasia caused by such coexisting diseases as influenza, pneumonia or tuberculosis is only one factor, and that there probably are other factors as yet unknown, of which possibly mechanical irritation, such as dust, may be a contributing factor." (page 6)

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(3027) Hodge Canada	"It is generally agreed that malignant disease of the lung is increasing. Various causes have been suggested for this increase. It has been thought, for instance, that the irritation of gasoline fumes and the inhalation of particles of tar may play a part." (page 60).
(3232) Kirklin Minnesota	A discussion of Kirklin's presentation by James T. Case of Chicago: "One cannot close this discussion without wondering if the author has anything new to present concerning the cause of the increased frequency of carcinoma of the lungs. I recall that in a recent discussion on this subject the idea was advanced that roads plus the increased use of the automobile resulting in more inhalation of tar products in dust might be one of the causes of the increase in the frequency of carcinoma of the lung." (page 99)
(3328) Gutteridge Australia	"Whether the tar-paving of roads has had any effect is problematical, but it is noted that the increased incidence of the disease in Australia is as belated as has been the conversion of water-bound macadamized roads to tar paving. It is also noteworthy that Iceland, being a hilly forest country, has very few roads or bridges, and the chief mode of transport is by pack-horse." (page 18)
(3420) Churchill Massachusetts	"Various causes have been invoked, among them inhalation of tar dust from the roads." (page 279)
(3417) Geschickter & Denison Maryland	60 case reports analyzed. "Radioactive substances, heavy oils and tar, and chronic inflammatory diseases of the lung are believed to be predisposing factors. The etiological significance of these agents, however, is not well established. Chimney sweeps, aniline and paraffin workers, and miners working with radioactive minerals have been known to develop the disease twenty or thirty years after exposure. The most conclusive series of cases from an etiological point of view are those reported among the miners of Schneeberg and Jachymov after long contact with radioactive ores." (page 857)
(3412) Bronfin Colorado	6 case reports. "Among several causes, Stivelman (2814) mentions the gasoline age and its production of deleterious gases." (page 193)

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(3621) Rosedale & McKay New York	"From a knowledge of local conditions it was estimated that 43 patients, or 75.4 per cent of the total number, were emloyed in occupations requiring exposure to dust or other irritating atmospheric factors. We feel that this may possibly be an etiologic factor in producing chronic irritation of the bronchial epithelium, resulting in protoplasia and metaplasia." (page 495)
(3736) Kenning Michigan	"The association of benzine products, such as asphalt, tar and motor gases has been noted. These factors may have some bearing on the relative increase of carcinoma of the lung. x x x Approximately 50% of our own cases were found in people of Polish and Slavic descent." (page 466)
(3918) Jenkinson & Hunter	Discussion of experimental carcinogenesis using tar. "The etiologic factors in bronchiogenic carcinoma as in carcinoma elsewhere, remain obscure. Chronic inflammatory process, inhalation of irritating substances and hereditary susceptibility are all invoked because of their possible contributory importance." (page 2392).
(3951) Lipowitz Canada	"The study of etiology of cancer thus comprises three distinct phases: intrinsic factor that causes tissue injury, an intrinsic factor which is the general susceptibility of the individual, and the transformation of the cell to a malignant status. Möller (2423) painted the backs of young rats with tar and did not produce carcinoma of the skin, but rather carcinoma of the lungs. Similar results were obtained with mice. It was believed that tar acts as a factor in lowering the resistance of mice, while the cancer is caused by the inhalation of irritants. The irritation in this case was due to the fact that the mice lived in burrows under sawdust and hay. Today, the irritation theory of Virchow is regarded as an essential factor in the aetiology of carcinoma of the lung." (page 10)
(3952) Anonymous AMA foreign correspondent in France	"For years a recrudesence of primary pulmonary cancer has been observed in France. Kling, Samsonov and Heros think that one of the causes of this increase is the tarring of roads. Statistics offer little to confirm the responsibility of tar. Kling and his collaborators do not propose to proscribe tarring but they would like to see employed only innocuous substances. Benzopyrine contained

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within the tar used nowadays has a high cancerigenic effect on animals, inducing cancers of the epidermal epithelioma type. Benzopyrine can be mixed accurately with tar. Its proportion is about 0.5 per cent. Since from 2 to 3 Kg. of tar is spread over a square meter, one can gage the amount of benzopyrine used. Benzopyrine adheres solidly to particles of silica and other materials spread over roads. The benzopyrine-impregnated dust raised by the wind can be borne a great distance from its source and carry with it the harmful tar. A certain number of substitutes for tar in use at present for the coating of roads, such as natural pitch and petroleum resin, do not cause cancer in animals." (page 245)

Group (b) Health hazards of occupational/environmental factors with tobacco smoking mentioned and no indications of preferential cause.

Authors Geographic Location	Results and Comments
(2931) Lickint Germany	"As generally known, in the search for the cause of this phenomenon, a number of causes have been considered (better diagnoses, frequent occurrence of influenza, automobile combustion, gas, street dust, road tar, war gas and others." (page 10 of English translation)
(3011) Bonner Georgia	"Chronic irritation may be considered one of the principal factors in the production of lung cancer. Some have believed the dusty air, the presence of gases from automobiles, the use of tobacco and the inhalation of particles of tar from the road beds to be possible etiologic factors. Konrad and Franke state that in Riga there has been a definite increase but that there has not been a coincident increase of automobiles and the use of tar in road building. Thus these factors could not account for the increase of lung cancer in this locality." (page 1045)
(3327) Pilcher & Brindley Texas	"Increase of tar in the air from roads, gas fumes from automobiles and industrial plants, and irritating stone dusts have all been discussed as possible factors in the increasing incidence of the condition. These ideas were furthered when Kimura (2321), reported the experimental pro-

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duction of pulmonary cancer in animals by the intratracheal insufflation of the lungs with coal tar. The great incidence of the condition among the cobalt miners in Schneeberg, Saxony, is proverbial. Increased smoking of tobacco has been mentioned also. None of these things have been proved to be significant. In our series it is interesting to note that five of the eight men patients were heavy smokers of cigarettes, although this may not be greater than any unselected group of men. We also note that of this group two had been for a long time restaurant cooks and one a baker. Another dated his symptoms from his work in an oil field, where he was exposed to fumes which were quite irritating to him. Two others had a history of chronic cough off and on for as long as they could remember. These findings, while suggestive, are not presented as proven etiological points in these cases." (pages 248-249)

(3645) Schrire
South Africa

"The etiology of carcinoma of the lung is obscure; attempts to produce it experimentally having up to the present failed. Some writers have tried to explain the recent increase in the recorded numbers by blaming petrol fumes, tarred roads, oil fumes and tobacco. The condition, however, is probably as common in South Africa as anywhere else in the world, and one has seen cases in people who have never been in a motor-car and who saw tarred roads for the first time on arriving at the Somerset Hospital for investigation." (page 475)

(3833) Faget & Harmos
Virginia

"Among the predisposing etiological factors various inflammatory lung diseases, such as influenza, bronchitis, bronchiectiasis and tuberculosis have been listed. Chronic irritation from the inhalation of smoke and dust has also been blamed. Arkin and Wagner (3613) found 90 percent of their patients were chronic smokers. All of our patients were heavy smokers. Jaffe believes syphilis, by causing a chronic irritation of the bronchial mucosa, may be of importance in the pathogenesis of lung cancer. Syphilis was present in 24 per cent of his cases. The inhalation of automobile exhaust gases and the emanations from tar on roads are other agents advanced to explain the growing incidence of pulmonary malignancies". (pages 22-23)

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(3929) Hochberg & Lederer New York	"Numerous theories have been advanced as to the bearing of inhalation of dusts or of tar from roads as a possible etiologic factor in carcinoma of the lung. No evidence of any such connection has ever been proved. Nor have tuberculosis, influenza, tobacco and war gases been shown to be etiologic agents. x x x. Kennaway and Kennaway (3632) have shown that the factors which lead to silicosis appear not be active in the production of cancer of the lung. They also have shown that in certain open air occupations in which there is exposure to the dusts of the road, the percentage of cases of carcinoma of the lung was high, whereas drivers of motorcars had a normal incidence. In this study they also showed that workers exposed to coal gas and tar tend to have a higher incidence of cancer of the lung." (pages 81, 82)

Group (c) Question health hazards of occupational/environmental factors with no mention of tobacco smoking.

Authors Gegraphic Location	Results and Comments
(3026) Boyd Canada	"The literature contains suggestions as to countless etiological factors. Of these only three need be mentioned - tuberclosis, influenza and the inhalation of irritating subtances. The first two have played no part in my own material. Regarding the third it is more difficult to be quite so definite, for the variety of possible irritants is great. It has been pointed out by numerous writers that the recent increase in the incidence of carcinoma of the lung coincides with the enormous increase in automobile traffic, the inference being that the inhalation of exhaust gases stimulates the bronchial mucosa to malignant growth. The widespread tarring of roads has been similarly blamed. In Western Canada there are no tarred roads, and most of the patients come from country districts where the contamination of the air by exhaust gases is negligible. I have never seen a case in a garage worker, although such a man is continually exposed to the waste products of gasoline in concentrated form." (page 240)
(3037) Maxwell & Nicholson Great Britain	"In the present series of London cases sixty-six were engaged in indoor and thirty-four in outdoor occupations. It must be remembered that a

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hospital in a large city draws its patients from a considerable part of the surrounding country, and the proportion of indoor to outdoor workers will vary with the proportion of city to country dwellers admitted. Also, we cannot be sure as to the length of time for which the occupation stated in the clincial notes had been followed, and we have to accept these statements at their face value; changes in occupation, recent or old, are not as a rule reflected in the notes, so that the classification is open to a very serious fallacy. Again, in many cases it is not easy to generalize as to the precise nature of some occupations on the lines of this classification, and such cases weaken the value of these figures. After careful consideration we have reached the conclusion that from our own figures, at least, there is no evidence to suggest that the outdoor worker is more liable to contract a bronchial carcinoma than his indoor colleague, and that the assumption of some atmospheric impurity to explain the increase in incidence of the condition is not justified by the evidence.

It must also be remembered that nearly the whole population spends so much of their leisure time nowadays in the open air that such possible aetiological factors as tar and road dust and fumes of oil and petrol are likely to be of almost equal importance in all irrespective of their occupation.

With regard to specific occupations, there was none which occurred with marked frequency in this series, nor post mortem was any occupational lesion found which might have been held to account, even in part, for the presence of the growth." (pages 21-22)

(3121) Peet
Great Britain

"Much also has been made of the inhalation of tar emanations as a possible aetiological factor, and although there has been an increase in the practice of tarring roads, there is insufficient evidence to justify correlating this fact with the increased incidence; nor has any association been found between the disease and tar workers. Ewing's (1919) dictum that in pulmonary carcinoma: 'The chief aetiological factor is pulmonary tuberculosis,' has not been confirmed by this study. In none of the cases was there evidence of pulmonary tuberculosis of an extent and character such as could be related to the carcinoma." (page 106)

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(3438) Sears Great Britain	"Exhaustive studies of the occupational incidence have been made, and, although the labouring classes appear to be most often affected, no occupation was found predominant. Many irritants such as road dust, tar and exhaust fumes have been suggested to account for the statement made by some observers that the disease is more common in outdoor workers, but as yet no definite conclusions have been reached, and the aetiology is as obscure as that of cancer in general. It can be said, however, that infection and other types of irritation do produce epithelial metaplasia which is suitable soil for the development of cancer." (page 106)
(3433) Edwards Great Britain	"As far as can be determined at present, occupation does not appear to be of any etiologic importance; and, although the previous history often contains evidence of influenza, bronchitis and pleurisy, it is more than probable that these are the first signs of the malignant changes in the lung rather than actual predisposing factors." (page 108)
(3530) Andrus New York	"A survey of the occupations of these patients yields nothing which might in any way be considered as of etiologic significance. Eighty per cent did inside work or desk work, while 20 per cent worked out of doors; of the latter there was one stonecutter, four were 'laborers,' three were farmers, one a gardener, and one a bricklayer." (page 236)
(3626) Rice Wisconsin	"The occupations of these patients also appeared to be of little significance. The distribution of indoor and outdoor work was similar to that of the hospital admissions as a whole and the number engaged in occupations with special hazards was no greater than for the unselected cases." (page 907)
(3815) Stein & Joslin Illinois	"Although an exhaustive study was made of the various occupations in this group, no conclusions of any significance could be drawn. At least 75 different occupations were represented, the largest group being farmers or common laborers. Eight, or 5 per cent, of the patients had been coal miners but 4 of these also had been employed

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in other occupations. In addition there were 2 patients whose occupations conceivably might have had some bearing upon the disease. One patient had worked originally as an ore miner, later as a metal plisher and motor assembler. A second patient had been employed for 7 years as an emery polisher inhaling fine particles of emery dust.

Rosedale and McKay (3621) state that 75.4 per cent of the patients listed in their group of 57 were employed in occupations requiring exposure to dust or other irritating atmospheric factors. It is difficult to evaluate properly the part that dust and irritative atmospheric factors play in the etiology of carcinoma of the lung, especially in patients coming from large cities or industrial centers. There have been no conclusive facts shown as yet to prove that the above are of major importance." (page 904)

(3812) Boyd
Canada

"These are nearly all based on the supposition that some carcinogenic agent is inhaled from the air, some agent which we owe to recent industrial and scientific advances. The favorite culprit is tarring of roads, an idea supported by the indisputed facts that tar when applied to the skin may produce carcinoma, and that inhalation of tar dust may produce cancer of the bronchial tree in the experimental animal. This is as reasonable as to say that cancer of the skin in man is usually caused by tar, or that the ingestion or inhalation of aniline dyes is the common cause of carcinoma of the bladder.

The material on which this paper is based represents a cross section of the city of Winnipeg and the province of Manitoba, a part of the country where tarred roads are remarkable for their absence. Nor can the inhalation of automobile waste products be a factor of importance in the great open spaces of the Western prairie. The disease is common in Russia where there is no tarring of roads and few automobiles. Dr. E. L. Turner, who spent ten years at Beyrut, Syria, assures me that cancer of the lung is as common there as in Philadelphia, yet most of his patients lived under the same conditions as did their forefathers in the days of the Pharaohs." (page 318)

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Group (d) Question health hazards of occupational/ environmental factors with mention of tobacco smoking.

Authors Gegraphic Location	Results and Comments
(3003) Davidson Great Britain	"Tobacco, war gas, petrol fumes, dust, and tar from the roads have all been subject to discussion as possible and likely sources of irritation, but it cannot be said that any observations have been made so far which justify definite conclusions as to the aetiological importance of these factors, and such control evidence as there is does not lend much support to the theories in its favour. The Brompton Hospital records do not add anything material to the facts furnished by the above investigations. Of the 107 cases, confirmed by autopsy, the occupational incidence was as follows: Housework (including married women, unmarried housekeepers and domestic servants), 11; labourers, 9; painters, 4; porters, 6; clerical work (L.C.C. clerks, civil servants, post-office clerks), 11; policemen, 2; travellers, 3; motor drivers, 2; chauffeur, 1; engine driver, 1; steam-wagon driver, 1; carman, 1; not recorded, 9. This makes a total of 61. The remaining 46 comprise all sorts of artisans and workers in different shops, stores, etc., railway officials other than porters, and various occupations not included under the above descriptions. After deducting from the total number the 9 cases where occupations were not recorded, the remaining 98 were divided into indoor and outdoor workers respectively, so far as it was possible to differentiate these, having regard to the fact that some of the occupations specified included workers in both classes, with the result that equal numbers were found (49 of each). Deducting the 18 females from the indoor workers, we have 31 indoor occupations to 49 outdoor occupations among the male cases. From this it can hardly be suggested that any special conclusion can be drawn as regards indoor and outdoor occupations in relation to the disease in question." (pages 34, 36-37)
(3222) Brockbank Great Britain	"An investigation of the occupations of 898 cases of primary lung cancer collected from the literature suggests that the labouring classes predominate, although no one occupation stands out. Poison war gas, tobacco smoking, road dust, and motor-car fumes are all possible aetiological

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factors. The occupations of sixty-two cases have been investigated in some detail. Nine (14.5 per cent.) seemed to have definitely dusty jobs, and eighteen (29 per cent.) worked amongst gases and fumes. Four were badly gassed in the war, and nine smoked excessively." (page 37)

(3212) Rogers
Austria

"A study of environment or occupation proved of little significance. The patients were all born either in Austria or in one of the adjacent countries, and were all from the working class. The number of years spent in large or small communities, factory centers, farming districts, etc., was not obtainable from the existing records. The occupations were varied, and were thirty in number. In only one patients was a history of a chronic cough as a result of his occupation noted. This patient was an upholsterer. The largest number in any one occupation was among the women, 6 being domestic servants. Of the 39 men only 5 could be said to have been subjected to more than the average amount of respiratory irritation, as far as their stated occupations were concerned. Irritating fumes of any sort, with the possible exception of tobacco, did not seem to play a role." (pages 1058-1059)

(3627) Fleckseder
Germany

"The profession of our patients does not seem to have had a significant influence on the development of BrCa. For painters, vascular damage caused by lead, for waiters and coffee makers, the harmful effect of tobacco smoke could play a role. The relatively large ratio of outdoor professions is somewhat noticeable and can possibly be attributed to the more frequent occurrence of different lung diseases in these profession." (page 4 of English translation)

(3603) Craver
New York

"Claims have been made, both for and against the etiological role of tobacco smoking in cancer of the lung. In 48 male patients with cancer of the lung who gave a statement about their use of tobacco, 31 or 64 per cent were classed as having smoked to excess. In 10 instances this history of heavy smoking was associated with the factor of an occupation that was probably irritating, in 3 instances with a history of repeated or severe respiratory infections, and in 4 instances with both an occupational factor and a history of respiratory infections. On the whole, these figures do not seem very impressive, and seem almost to

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call for the assumption of some additional factor of special susceptibility of the bronchi to forms of irritation that are probably present to an almost equal degree in subjects who do not develop cancer of the lung." (page 351)

(3724) Husted & Biilmann
Denmark

"With regard to the significance of the noxious influence of some particular occupations, the present material offers absolutely no suggestion of that kind. These patients, eight women and 27 men, came from all classes of society and represented a quite accidental mixture of all occupations, without predominant frequency of any occupation or group of workers. It is quite true that no mining is done in this country, but apart from one patient who was a stoker the material contains no cases in which it would be reasonable to assume that the patient had been exposed to the effect of dust and smoke more than all other persons in general. In this connection it is also to be mentioned that any marked degree of anthracosis of the lungs was found in two cases only. Tobacco has frequently been discussed as an etiological factor, but our patient material includes no tobacco workers, and according to the case records only four of the patients were particularly heavy smokers." (page 351)

(3705) Frissell & Knox
New York

"In our series of cases occupation did not play a significant part. There were no miners in the series and only 3 were engaged in dusty trades - a bricklayer, baker, and fireman. Neither were the habits of the patients of significance, except for the well-nigh universal use of tobacco. One had been a victim of war gas. Ten of the cases were in females, 36 in males." (page 223)

(3855) Frank
Colorado

"Chromates and tobacco smoke have also been implicated. Carcinogenic agents have been studied extensively. 'For many years it has been known that a variety of agents are capable of inciting malignancy (Andervont). Among these are the sex hormone estrin, benzopyrene, an azo-compound (o-amido-azo-tuluol) and 1.2,5,6-dibenzanthracene. Since 1930, approximately forty-five definite chemical compounds have been discovered which are capable of eliciting tumors in experimental animals. Up to the present, there is no possibility of arriving at any generalization regarding molecular structure necessary for cancer inciting properties. The only property common to the

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various compounds is the presence of at least two benzene rings. It has been found that the lungs of one particular strain of mice are delicate test objects for the carcinogenic activity of 1,2,5,6-dibenzanthracene; for, in so far as macroscopic evidence is concerned, the pulmonary tumors appeared earlier than those arising at the site of subcutaneous injection. The fact that tumors appear in the lungs of some mice following the subcutaneous injection of 1,2,5,6-dibenzanthracene may be of interest, for it suggest that inhalation of carcinogenic agents may not be essential for the development of some pulmonary tumors of other species.

According to the Kennaways (3632), workers exposed to coal gas and tar, and those engaged in the preparation and sale of tobacco, tend to show an increased prevalence of cancer of the lung. Occupations concerned with the supply of alcohol have a high incidence of cancer of the larynx. No evidence has been found that tarring of roads has affected the incidence of cancer of the lung in the general population. Such data as are available suggest that coal tar in the atmosphere from any source does not readily give rise to this condition." (page 469)

The above list does not identify the sepcialty of authors but this can be derived by re-examining the articles. It may prove enlightening to determine the specialty of authors who question environmental/occupational factors and do not mention tobacco smoking. Boyd, a Canadian pathologist who wrote a textbook on human pathology, also wrote two articles eight years apart (3026, 3812). He, and possibly other contemporaries, appeared to have favored intrinsic or hostal predisposition factors, and questioned the importance of extrinsic factors, environmental/occupational, as well as tobacco smoking.

Lung cancer deaths in Sheffield tradesmen. Turner and Grace analyzed twelve occupational groups of males in Sheffield, England, from 1926 to 1935 inclusive. Lung cancer comprised 9.6 per cent of 3861 cancer deaths. The

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following groups showed significantly greater lung cancer mortality: foundry workers and smiths, grinders, engineers and transport workers; compared to mortality experience by clerks, business and professional men (3811). These observations confirm essentially those of Duguid (2721) and the Kennaways (3632).

Lung cancer deaths in U.S. veterans. Nolan reviewed 1250 autopsy records of the Veterans Administration from 1921 to 1932. Lung cancer deaths were 0.88 percent of all autopsies, and 9.2 percent of all cancer deaths (3211). Matz reviewed records up to 1937 and noted that lung cancer deaths were increased to 2.4 percent of all autopsies in 1932, and 5.3 percent in 1937 (3856). Of the 138 lung cancer patients, 36 percent gave a history of being connected with occupations or industries in which there was a possibility of irritation and traumatization of the respiratory tract. The fact that so large a percentage had been engaged in occupations which caused respiratory tract irritation was supportive of occupational etiology of lung cancer.

Japanese Research on Experimental Carcinogenesis.

The positive results reported from Japan were cited by Harris as to why American tobacco companies should have conducted research on lung cancer. Before Pearl Harbor, Japanese scientists published through Nipponese medical journals that were rarely read by Americans. For the benefit of Westerners, important medical developments were contributed to German journals and occasionally in American or British publications. In 1937, Kinoshita summarized the studies on 'cancerigenic' chemical substance conducted by

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Japanese investigators. The chronology of events derived from Kinoshita's review and other sources was as follows:

1905 Yamagiwa proposed that "repetition or continuation of chronic irritation may cause a precancerous alteration in epithelium previously normal." (see ref. 1814)
1914-1918 Yamagiwa & Ichikawa confirmed Yamagiwa's hypothesis by painting coal tar on rabbit ears for 70 to 150 days resulting in metastasizing epithelioma (1513, 1814).
1923 Kimura reported adenocarcinoma in guinea pig lung following intra-bronchial insufflation of coal tar (2321).
1930 Arai & Kikitsu reported lung cancer cases but no information on smoking habits (3038).
1931 Chikamatsu tested tobacco tar in rabbits and mice (3129).
1932 Yoshida reported hepatic cancer in rat following oral administration of o-aminoazotoluene (Cited in 3711).
1937 Taki tested substance isolated from tobacco tar (3737).
1937 Kuroda reported coal-generator gas workers developed lung cancer (3738).
1937 Kinoshita reported hepatic cancer in rat following oral administration of butter yellow or N-methylated compound of o-aminoazotoluene (3711).

I personally would have doubted the credibility of Kinoshita's report if his article was read after Japan occupied China and Southeast Asia (see pp 47, 48 above). Taki "collected tobacco tar from Japanese tobacco pipe which was first dissolved in ether and filtered, and then this ether solution, after shaken with hydrochloric acid and repeated with water to eliminate pyridin, nicotine, etc., was separated and condensed by evaporation. The product was applied twice weekly to the skin of mice. During the experiment the number of animals was increased on several occasions, until the total number was 104.0 of this number, 94 died in 100 days or less. Out of the surviving 10, five have already passed the 130 day mark, two of which shows cancers and the other three papillomas. In one case the first papilloma was noticed after 85 days." This is Kinoshita's description of Taki's experiment that was subsequently published in Japanese (3737); an English translation has become available. Kinoshita has characterized Taki's results as indicating that "tobacco tar" showed

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"high carcinogenic potency" but he did not mention any reference compound for comparison. A Japanese scientist is needed to translate the articles published prior to, and after 1937. There are reports on experimental carcinogens such as: constituents of coal tar, constituents of tobacco tar, hormones, cholesterol, sugar-tar, and pityrol (tar residue formed during polishing of rice). The available information suggested that Japanese scientists by 1937 suspected coal tar as a pulmonary carcinogen based on animal experiments and lung cancer among coal gas workers. As to smoking and lung cancer, I could not find articles by Japanese on smoking habits of lung cancer patients. Arai and Kikitsu reviewed 4,663 autopsy records from "34th year of Meiji or 1901, to the 15th year of Taisho or 1926", or starting a quarter century before the ascendency of the late Emperor Hirohito. Lung cancer in Japanese was 2.6 percent of all cancer cases, whereas European figures during the same period exceeded 10 percent. Arai and Kikitsu reported that there was one case associated with external injuries to the chest, two followed influenza, and three were employed in dusty occupation (3038). There was no mention of smoking habits. The authors cited European publications relating to dust inhalation and lung cancer i.e. Hampeln (2328), Schmorl (2329), and Uhlig.

European Research on Experimental Carcinogenesis.

The animal experiments needed to support the coal tar hypothesis were conducted at research laboratories in Europe. There were six laboratories in Great Britain, one in Scandinavia and another one in France. During the 1930's, the Germans were no longer active in animal coal tar experiments and instead directed their interest to "tobacco tar". It was rumored that the sale

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of tobacco, monopolized by Jewish merchants, had to be discouraged by Nazi physicians, disguised for health reasons (see Chapter IV).

Research Institute of the Royal Cancer Hospital, London. Unlike the Cancer Research Institute headed by Roffo in Argentina, the policy at the London Institute was to have scientists publish under their own names: E.L. Kennaway, I. Hieger, J.W. Cook, C.L. Hewett, G. Barry, G.A. Haslewood, W.F. Mayneord, W.E. Bachmann, A. de Dansi, C.G.M. de Worms and A.M. Robinson. The chronology of their accomplishments was as follows:

(2415) Kennaway	Reviewed literature on chemistry of seven forms of tar reported to produce skin cancer in workers.
(2416) Kennaway	Isoprene heated 720 to 920 C.
(2517) Kennaway	Yeast, human skin, Durnham coal, California petroluem, isoprene and acetylene heated 720 to 929 C.
(2524) Kennaway	Anatomical distribution of occupational cancer.
(2825) Kennaway & Sampson	Cholesterol heated.
(3039) Kennaway	Aluminum chloride added to tetralin, acetylene, xylene, naphthalene, bromobenzene and tetrahydro-naphthalene, pure synthetic 1:2:7:8-dibenz-anthracene.
(3040) Kennaway & Hieger	Fluorescence spectra bands at 4000, 4180 and 440 Au. for most carcinogenic materials.
(3233) Cook, Hieger, Kennaway & Mayneord	Test for skin-cancer producing action on mice for polycyclic aromatic hydrocarbons including dibenz-antracene.
(3333) Cook, Hewett & Hieger	Isolated and synthesized skin-cancer producing hydrocarbons from coal tar including benzpyrene.
(3544) Barry, Cook, Haslewood, Hewett, Hieger & Kennaway	Isolation of tetracyclic and pentacyclic hydro-carbons from coal tar.
(3739) Hieger	Fluorescence spectrum of 3,4-benzpyrene.

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(3740) Bachmann, Cook, Dansi, de Worms, Haselwood, Hewitt & Robinson	Derivatives of methylcholanthrene, benzanthracene, benzpyrene and benzphenanthrene.
(3741) Cook, Haslewood, Hewett, Hieger, Kennaway & Mayneord	Review chemistry and experimental carcinogenicity of polycyclic aromatic hydrocarbons.

I have rated the above record of accomplishments as the most outstanding for the 1920's and 1930's. It should be noted that Harris used three of the 13 above articles and concealed the purpose and outcome of the studies. The overall purpose of Kennaway and his collaborators was to develop chemical (fluorescence) and biologic (mouse skin painting) tests for identification of carcinogenic compounds in coal tar. They were able to identify the most active cancer-producing compounds yet encountered as belonging to the cholantherene group and were of special interest on account of their structural relationship to bile acids. The carcinogenic properties of 3,4-benzpyrene, a constituent of coal tar, and 1.2-benzanthracene derivatives were described. However, the group lamented that "little progress has been made in elucidating the mechanisms of cancer production by chemical compounds," although they enumerated a number of genetic and other factors that influenced carcinogenesis such as hormones, diet and radiation.

> "The results obtained in the last few years have shown that a variety of tumours, as carcinoma of the skin, kidney, testis, bladder, liver, and uterus and sarcoma of the subcutaneous tissue, peritoneum and spleen, can be induced by pure chemical compounds and doubtless many of the negative instances collected under heading VI, p. 235, will be eliminated by the use, either of known compounds in other media, or of compounds not yet tested, or not yet synthesised. All these results indicate that the variety of tumours which occur naturally in different organs, and in different species, might be due to the production under conditions of disease of a variety of carcinogenic chemical compounds. But the mere fact that one can imitate a natural process by the use of an artificial agent does not of course prove that one has discovered

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the actual agent by which the natural process is brought about. Thus, many compounds will produce oestrus, and it is certain that some of them at least are not the causes of natural oestrus. Again, calciferol is antirachitic, but there is now evidence that it is not the antirachitic substance occurring normally in animals. Hence, the line of investigation that now requires to be followed in cancer research is not so much the production of tumours by artificial means as, what is incomparably more difficult, the discovery of the actual factors by which the naturally occurring tumours are induced.

The high incidence of experimental cancers induced by many workers in different parts of the world in an appropriate tissue and species under the influence of one of the more active carcinogenic compounds, as benzpyrene or methylcholanthrene, suggests that the introduction of some extraneous factor is not essential for the onset of cancer, although one would not deny that such factors may exist, and may give rise to some forms of cancer.

The increase in the frequency of a naturally occurring form of cancer, as, for example the occurrence of cancer of the lung in 20 per cent instead of in 5 per cent of mice, in the presence of a known carcinogenic agent suggests that this agent can summate with the unknown, naturally occurring carcinogenic factor to give an effective stimulus. Burrows has evidence (in course of publication) that in the rabbit the incidence of cancer of the uterus can be affected in the same way. This summation of causative factors suggests very interesting possibilities in the study of cancer.

Investigation of the chemical carcinogenic agents, which were the outcome of studies of industrial cancer, has been carried a stage nearer the realm of normal biological phenomena by the demonstration of a structural relationship between certain of these compounds and normal constituents of the human body. The laboratory transformation of bile acids into methylcholanthrene suggests the possibility of such changes occurring in the body, and doubtless many workers will consider such possibilities in connection with future investigations concerning the formation and degradation of cholesterol in the animal organism.

Attention has been directed already to our ignorance of the mode of action of the chemical carcinogenic compounds in producing cancer. Obviously it is desirable that investigation of the problem should be pursued, both from the point of view of obtaining a better understanding of the nature of the malignant change, and also in connection with the search for therapeutic agents against cancer. The use of pure chemical carcinogenic compounds should materially assist such studies on account of the certainty with which malignant tumours may be induced by these agents under exactly defined and reproducible conditions." (pages 242-243 of ref. 3741)

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The summation theory was not pursued by Campbell but will be discussed further when environmental carcinogens are individually reviewed (Part Four).

National Institute for Medical Research at Hampstead. Harris quoted two of ten publications by J. Argyl Campbell on the subject of experimental carcinogenesis in mice. The pertinent publications were as follows:

(3636) Campbell "It is shown that carbon monoxide breathed for prolonged periods (one-third of life) retards, but does not prevent, development of tar cancer in mice. There is no evidence herein in favour of the hypothesis that the recently reported increase in human cancer is connected with the presence of carbon monoxide in the air of streets, garages, factories, kitchens, etc. Breathing oxygen at 60 per cent. of an atmosphere has no effect upon development of tar cancer in mice." (page 245)

(3453) Campbell "Mice were repeatedly exposed to dust obtained by sweepings from tarred roads and containing about 2 p.c. of tar. Cancer of the skin developed in 70 p.c. of those surviving long enough. The incidence of primary adenoma of the lung was increased to tenfold that of the controls: the lungs of the dusted mice contained much dust. The breathing of carbon monoxide, if anything, retarded the effects of dusting.

The bearing of this research upon the debated increase in tumours of the human lung cannot be assessed at present. The mice were exposed to much more excessiving dusting than occurs with human individuals. Cleanliness prevents cancer of the skin in man, and the natural mechanism for removal of dusts from the healthy lung may suffice for the small amounts of dust inhaled.

There is the further question whether these tumours of mice may be compared with those of the human lung. The experiment with mice is to be repeated and attempts will be made to transplant some of the tumours; the effects of dust, with the tar products removed, will also be studied." (page 294)

(3642) Campbell "1. Mice were exposed for 7 hours on 5 days each week during most of the lives to exhaust gases from internal combustion engines in concentrations somewhat resembling those obtaining in traffic blocks and garages. There were no marked effects upon the well-being of the mice. Carbon (soot) and lead were excluded in these experiments.

2. Mice were similarly exposed to fumes and tarry matter from cigarette smoke without any marked pathological effects.

3. The incidence of primary lung tumours in mice is considered in detail. These tumours are usually rare before

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the latter half of the second year of life. Exposure to exhaust gases has little effect upon this incidence when compared with the controls. The incidence for the tobacco group of mice is on the high side, but these mice survived longer than the other groups.

4. The incidence is increased by dust collected from tarred roads, as shown previously. Some of these tumours are definitely malignant in appearance. It is not known yet whether the dust freed from tar has any influence; this question is under examination, and the results should be available in a few months. Age and heredity have an influence on the incidence of these primary lung tumours of mice, but these factors are not responsible for the result with the tar dust. This dust contained much more tar than the tobacco smoke." (page 157-158)

(3742) Campbell

"(1) Some evidence has been obtained recently both from human statistics and experiments with mice that road dusts (with and without tar) and other dusts increase the incidence of lung tumors. In mice the increase is higher when the tar is also present in the dust.

(2) Gases and fumes from internal combustion engines under ordinary circumstances do not influence the incidence of lung tumors. Motor vehicles may however play some part by constantly stirring up the fine road dust.

(3) Some statistics indicate that workers with tobacco are liable to cancer of the lung and larynx. Some animal experiments give evidence that tobacco smoke and fumes may cause a slight increase in incidence. Further work is required, but this factor does not appear so important as the road dust.

(4) Animal experiments indicate that heredity may play an important part in susceptibility to lung tumors. The susceptibility may be increased by subcutaneous injection of certain agents. Even here it is suggested that the irritant or stimulus to start the tumor comes from the external environment. Under ordinary conditions this stimulus may be below the threshold.

(5) The earlier work with animals was of too short a duration to obtain undeniable evidence regarding the effects of dust etc. upon the incidence of lung tumors and more experiments of a prolonged nature are required. Lung tumors are late in development.

(6) So far as the evidence goes it supports the 'irritant' theory for cancer of the lung and indicates that there may be several irritants - coming from the external environment - and several factors e.g. heredity capable of exerting an influence.

(7) There is no substantial reason why the results for experiments with mouse lung tumors should not be applied to man." (pages 456-457)

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(3743) Campbell "(1) It was shown previously that dust from tarred roads causes cancer of the skin of mice. Road dust minus tar, as removed by benzene, does not cause cancer of the skin of mice; it stimulates the production of lung-tumours in mice, but not to so great an extent as when the tar is also present. Lung-tumours are rare in mice before they are 12 months of age.

(2) The dust does not cause any obvious inflammatory reaction - apart from the tumours themselves - in the lung or lymph-glands.

(3) Perhaps the presence of lung-tumours amongst some of the control mice is due in part to the dust breathed from the contents of their boxes or from the general atmosphere. This dust may contain a carcinogenic agent, e.g. tar, or it may 'irritate' the lung without obvious inflammatory reaction.

(4) Tar, either by a direct action on the lung itself or indirectly by some action on other tissues, or both, stimulates the production of lung-tumours in mice and hastens their appearance.

(5) Metastases from lung-tumours in mice are recorded, for the first time in this country, so far as we know. The majority of the lung-tumours in the dusted mice are malignant." (page 223)

(3857) Campbell "Sir, - With reference to the recent annotation (Br Med J March 26, p. 682) on the subject, some further information may be of interest. In some respects it is possible to bring the Joachimstal (and presumably Schneeberg) miners' lung cancers into line with those observed in metal grinders and in the mice exposed to road dust. In all cases, besides silica in some form, iron is present in the dust. Some of the inorganic contents of the Joachimstal dust resemble very closely those of the road dust, which produce lung cancer in mice. The presence of some form of iron and silica in these dusts is suggestive, and further experimental work is in hand dealing with this aspect of the problem." (page 955)

(3953) Campbell "(1) Tarry matters from the following have been tested for carcinogenic potency, using the mouse-skin test: Dusts from tarred roads; cigarette smoke; chimney soot; soot from exhausts of internal combustion engines burning heavy oil; a binding material in cardboard.

(2) As proved by the production of skin cancer, the tarry matter from tarred roads contains potent carcinogenic agents as does chimney soot, but under ordinary conditions the effect of the latter in its action on the skin seems to be mitigated somewhat by the presence of the carbon of the soot, while the effect of the former seems to be aided by the presence of inorganic constituents.

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(3) Cigarette smoke, under ordinary circumstances, gives rise to tarry matter which may occasionally produce hyperplasia and cancer of the skin after prolonged application.

(4) Tarry matters from the motor-exhaust soot and from the cardboard tested do not produce cancer when painted on the skin of mice.

(5) Exhaust soot suspended in the atmosphere slightly increases the incidence of lung tumours in mice, while chimney soot does not produce any noticable increase. The dust from tarred roads appears to be the most dangerous source of carcinogenic agents; when inhaled it gives the highest incidence of lung tumours in mice. It is considered that here again the inorganic constituents in this dust (for example, silica, iron) enhance or aid the effect of the tar, while, on the other hand, the carbon of soot tends to mitigate any effects of the tar present in producing tumours of the lungs. Irritation without inflammation appears to play a part in genesis of these tumours both in control and experimental mice.

(6) Although some primary lung tumours in mice are simple adenomata, other tumours reveal characters of typical malignancy with production sometimes of metastases. Further examples of metastases have been obtained." (page 131)

(3954) Campbell [Response to annotation in Lancet, see below]

Harris misunderstood Campbell's interpretation of the experimental results, probably because he examined only two publications (3642, 3953). Even the two he selected did not specifically state that cigarette smoke was a cause of lung cancer. A reading of an annotation in Lancet would have avoided the confusion (3643).

"In the present experiment the mice, on the per kilo basis, were exposed to conditions resembling at least those of a more than moderate cigarette smoker. Nevetheless there was no effect of any importance upon death-rate, body-weight and rate of growth of mice. There were 17 experimental mice and 11 control mice with primary tumours of the lung; the increase in the case of the former will be discussed later. Three of the experimental females showed mammary carcinomas. The other pathological changes resemble those given for the mice in Exp. A and are of no obvious significance. Fertility was tested, and there was no change compared with the controls.

Although suggestive, we do not consider that the incidence of lung tumours in the cigarette smoke experiment is high enough above that for the controls of the same age - 919 days - to demand special attention, because the increase is due to mice which

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survived longer than those of any of the other groups (pages 154-156 of ref. 3642)

The second paper quoted by Harris contained the following paragraph, reiterating that lung tumors appearing after skin painting were related to spontaneous appearance because of aging:

> "'Tar' from cigarette smoke. - Cigarettes were smoked artificially (Campbell, 1936) and the hot smoke was passed through a cool glass tube, in a side bulb of which some of the substance of the smoke condensed to form a dark brown liquid. This was concentrated and painted on the skin of 23 mice in the usual way, twice a week for 20 months. In one case a typical epithelioma developed, the wart being first noticed after 16 months of painting. In another of these mice which had been painted for 20 months the painted area of the skin at death was much thickened, and on section revealed the typical hyperplasia, which represents the first stage of cancer reaction to tar painting. The tarry matter used had not been exposed to a temperature higher than that produced in cigarette smoked in the ordinary way. Compared with the road tar this tobacco 'tar' is certainly not very active, but it apparently may give rise to cancer of the skin after prolonged application.
>
> Seven, or 35 percent., of the 20 mice living 10 months or longer and painted with cigarette 'tar' exhibited primary carcinoma of the lung. Twelve of these mice lived for 2 years or longer - that is, to an age favourable to the development of lung tumours." (p 126, ref. 3953)

Campbell took the opportunity in response to the annotation in Lancet, to justify the use of mice in the investigation of pulmonary carcinogenesis:

> "Sir. - The annotation on p. 521 of your last issue implies that mice are more susceptible than other laboratory animals to spontaneous tumours of the lung. This may be more apparent than real. Other laboratory animals are killed usually early in life, while mice, which live only about two years, are far more frequently allowed to fulfil their allotted span of life. Since tumours of the lung in mice and man are most prevalent during the last quarter of full life, it is probable that the same will hold for other animals. At any rate it has not yet been determined for them one way or the other to my knowledge. Moreover inbreeding in mice is much more common.
>
> Again you state that mice are more susceptible to carcinogenic tar than other animals. This may be due merely to the fact that in tar-painting experiments the painting usually covers only up to six months. This period is about one quarter, or a large

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fraction, of a mouse's life, but a much smaller fraction for other laboratory animals. For a fairer comparison tar-painting should be prolonged for a quarter of their full lives also. Further so far as the evidence goes the skin of man is as susceptible to tar as is that of the mouse. This is why I chose mice for my dusting experiments.

Your statement, that the conclusion from my dusting experiments is that the tar in the road dust is responsible for the increase in incidence of lung tumours, needs some adjustment. My paper, mentioned by you, indicates that tar is only one of the factors, since the road dust still causes a definite but smaller increase in incidence of lung tumours when the tar is removed from it. I certainly have not put so much emphasis on the part played by the tar alone. The inorganic constituents are under suspicion as well, both for man and mice, and are being tested in mice. My results also support to some extent the irritant theory of cancer, the irritation or stimulation or disturbance of the cells being due to the continual presence and addition of a particular dust. Thus constant activity is required on the part of the phagocytes and lymphatics of the lung. There is otherwise no inflammatory reaction. A cause of cancer may be prolonged irritation without inflammation.

Certain statistics for human lung cancer support my findings for mice and I do not understand why Valade should conclude that my results for mice cannot be applied to man merely because, as he states, he could not produce cancer of the lung in 50 rats by intratracheal injections of methylcholanthrene; moreover in some cases sarcoma of the trachea was produced. With other technique the result might be different and tumours be produced in the lung as well. Valade does not mention Möller's research (2423) wherein he obtained cancer of the lung of rats by tar-painting. So far as I know, it was only a year later that the same results was established for mice (Murphy and Sturm (2520)). This does not support Valade's statement that it is easier to produce lung tumours in mice than in rats or other animals. I have concluded other experiments with mice using other different dusts and soot, and I do not always find it easy to increase experimentally the incidence of lung tumours in any strain of mice. These result add weight to the more positive results with road dust: they will be published shortly." (pages 603-604 of ref. 3954)

The above letter explained one of several reasons why American scientists emphasized selection of mouse strains for experimental pulmonary carcinogenesis. The debate on relevance of animal experiments to human cancer continued up to the present, although recent exponents of "Valade" have become less vocal.

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British and other laboratories. With the exception of Watson and his colleagues from the University at Sheffield who studied skin tar tumors in rats (3334) and mice (3041), the other investigators used only mice. Twort & Twort from Manchester University, tested over a hundred samples of mineral oils including shale oils, petroleum oils, and mixtures. They reported that potency measured by skin painting response was related to intensity of fluorescence (3130, 3454). Mottram from the London Radium Institute, reported that precancerous lesions induced by benzpyrene became malignant as a result of irradiation (3546, 3762, 3859). Castration did not influence susceptibility of mice to sarcoma cause by subcutaneous injection of methylcholanthrene (3744). Mouse exposure to air-borne dust was being studied at the University of Birmingham and results were not available during the 1930's (3860).

American Research on Experimental Carcinogenesis.

In the United States, the emphasis in experimental cancer research was on the selection of an appropriate animal model. All available publications during the 1930's were on mice subjected to either inhalation of coal tar or to injection of a potent carcinogen previously studied by mouse skin painting. Seelig and Benignus from the Barnard Free Skin and Cancer Hospital at St. Louis, exposed mice to soot by mixing the powder with the bedding of cages (3648, 3861, 3862). The Bar Harbor black strain mice known to be resistant to lung tumors, had a spontaneous incidence of less than 1 percent. A 10 percent mixture of gas-work tar in lampblack failed to induce lung tumor in contrast to the positive results from exposure to chimney soot. Unfortunately a

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susceptible strain was used in the latter experiment so that the testing results could not be compared.

Shimkin, from Wolcott Gibbs Memorial Laboratory at Harvard University, used intratracheal administration of hydrocarbons. About 90 percent of Strain A mice developed lung tumors within four months after the intratracheal injection of 0.1 mg. of 1,2,5,6-dibenzanthracene or methylcholanthrene dispersed in 0.1 cc. horse serum and cholesterol. However, since the procedure alone caused 35 percent mortality, the intratracheal administration was discarded in favor of intravenous injection (3956).

Andervont & Lorenz, from the USPHS Office of Cancer Investigations at the Harvard Medical School, selected a standard procedure, i.e., subcutaneous injection of 1,2,5,6-dibenzanthracene-lard solution to mice of several strains. From 1935 to 1939, nine articles were published with the following summaries:

> 1. "The presence of lung tumors in mice following the subcutaneous injection of dibenzanthracene-lard solution cannot be explained at this time. Practically all the lung tumors appeared in strain A or stock mice. The only common factor of these mice is their albino coat color. The mice of strain A are of pure stock and show a tendency toward the development of spontaneous tumors, but the ordinary stock mice used in this laboratory rarely develop spontaneous growths. While it is known that mice of strain A do possess a tendency toward the development of lung tumors, routine autopsies of these animals reveal very few such growths. No instance of lung tumor has been found in 100 routine autopsies of the stock mice.
>
> Microscopic examination of lung growths showed that practically all were carcinomas, regardless of whether the mouse had a subcutaneous sarcoma or no tumor at the site of the dibenzanthracene-lard injection. Thus, it may be assumed that the lung growths are primary tumors. The problem concerning lung tumors is receiving further consideration." (pages 1216-1217 of ref. 3548)

> 2. "In these experiments mice of strain A were given subcutaneous injections of a lard-dibenzanthracene solution. It was found that more of these animals developed lung tumors than subcutaneous tumors and, in addition, that the lung tumors arose earlier than did the subcutaneous growths. Hence it would appear

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that the lungs of these mice were more delicate test objects than the subcutaneous tissues for the carcinogenic activity of 1,2,5,6-dibenzanthracene.

The reason for the appearance of lung tumors in mice painted with tar or injected with carcinogenic compounds is unknown. The observations recorded in this paper indicate that in strain A mice the lung response occurred in a relatively short period of time. While it does not appear likely that 0.8 mg of 1,2,5,6-dibenzanthracene in 0.2 cc of lard was capable of altering the body state of mice to such an extent that lung tumors arose so much earlier than under normal conditions, it is not impossible that very small amounts of a carcinogenic agent left the site of injection and came into contact with the tissues of an organ which are known to be extremely susceptible to tumor growth." (page 220 of ref. 3745)

3. In this experiment 21 females of strain A were bred to males of strain C 57 black, and 21 females of strain C 57 black were bred to males of strain A. The mice of strain A are known to be susceptible to both spontaneous and induced lung tumors, while the mice of strain C 57 black are known to be very resistant to the development of all spontaneous growths, and in this laboratory no lung tumors have thus far been induced in them by the subcutaneous injection of a lard-dibenzanthracene solution. The progeny of this mating has been designated as the first hybrid generation. Females ofthe first hybrid generation were mated to the brothers to procure mice designated as of the second hybrid generation.

The absence of lung growths in a high proportion of uninjected controls of both the first and second hybrid generations shows that the lung nodules in the injected mice did not arise spontaneously and, in addition, shows that the lungs of the 62 second generation mice killed on July 23, 1936, were more responsive to the induction of tumors than the subcutaneous tissues, for 43 had multiple lung tumors without any evidence of a subcutaneous growth. This finding is similar to the results obtained in other experiments with strain A mice.

The presence of lung tumors in a high percentage of animals of both the first and second hybrid generations shows that the susceptibility of this organ to tumor formation induced by the subcutaneous injections of a lard-dibenzanthracene solution is inherited in a dominant manner." (pages 313-314 of ref. 3746)

4. "Seven pulmonary tumors arising in strain A mice which had received 1,2,5,6-dibenzanthracene parenterally have undergone from 3 to 23 serial passages in the subcutaneous tissues of normal mice. Three of the tumors consisted of carcinomatous elements mostly in the primary tumor as well as in the earlier passages, and all three have changed into sarcomas in subsequent passages. One other tumor has retained its carcinomatous structure through eight animal passages. It is suggested that the three tumors

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exhibiting a change in their histological appearance arose as mixed tumors induced by the direct action of a carcinogenic agent upon both epithelial and connective tissue elements in the lungs." (pages 354-355 of ref. 3747)

5. "Dog-serum and horse-serum dispersions of 1,2,5,6-dibenzanthracene were injected intravenously or subcutaneously and lard solutions of the same compound were injected subcutaneously into pure strain mice. The serum dispersions, when injected intravenously, induced lung and liver tumors, and when injected subcutaneously, produced local tumors at the site of injection as well as lung and liver tumors. Lard dispersion, when injected subcutaneously, evoked local tmors at the injection site and also produced lung and liver tumors.

The appearance of lung and liver tumors in mice injected subcutaneously is evidenced that 1,2,5,6-dibenzanthracene is capable of producing tumors in tissues which are distant from the site of injection." (page 646 of ref. 3748)

6. When 1:2:5:6-dibenzanthracene was adsorbed on charcoal and injected subcutaneously into strain C3H mice, it produced tumors at the injection site. When charcoal was added to a horse-serum dispersion of 1:2:5:6-dibenzanthracene and the resulting mixture injected subcutaneously into strain C3H mice, tumors arose more rapidly at the injection site than in control mice injected subcutaneously with the horse-serum dispersion. Induced lung tumors were found in mice injected with the horse-serum dispersion but such tumors were not observed in mice injected with the horse-serum dispersion to which charcoal had been added. These results suggest that charcoal held the carcinogenic compound at the site of injection. When dibenzanthracene charcoal was injected subcutaneously into strain A mice, it induced tumors at the site of injection in but a few mice, which indicates that the subcutaneous tissues of mice of strain A are more resistant than those of strain C3H to the carciogenic action of dibenzanthracene charcoal. Subcutaneous injection of dibenzanthracene charcoal into strain A mice induced very few, if any, lung tumors which is evidence that the dibenzanthracene was held firmly by the charcoal. This is regarded as further evidence that lung tumors are induced in mice by a direct action of the cacinogenic agent upon the lung tissues." (page 1939 of ref. 3749)

7. "Reciprocal breeding was carried on between mice of strains C3H and I and strains C3H and Y. The female parent mice and most of the hybrid mice were injected subcutaneously with a lard-dibenzanthracene solution. The results of the investigation may be summarized as follows: (1) The C3H female parents were more susceptible to the carcinogen than either the I or Y female parents; (2) The hybrid mice were of intermediate susceptibility when compared with the susceptibility of the parent strains; (3)

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Hybrid mice derived by mating strain C3H to strain I were considerably more susceptible to induced pulmonary tumors than those derived by mating strain C3H to strain Y; (4) Female hybrids born to C3H mothers and I fathers were more susceptible to spontaneous mammary cancer than female hybrids born to C3H mothers and Y fathers." (page 1670-1671 of ref. 3863)

8. "Hepatomas occur spontaneously in strain C3H mice. Eighty-five female mice one year of age or older exhibited an incidence of 11.7 percent at an average age of 16.9 months, while 80 males in the same age group had an incidence of 22.5 percent at an average age of 15.1 months. Pulmonary tumors also occur spontaneously in strain C3H mice but their incidence in mice over one year of age (7.2 percent in 165 animals) is lower than the incidence of hepatomas. Primary pulmonary tumors can be induced in strain C3H animals by the subcutaneous or intravenous injection of dibenzanthracene. Injection of the hydrocarbon hastens their appearance and increases their number. Definite conclusions are not justified as to whether hepatomas are induced by dibenzanthracene or methylcholanthrene." (page 1168 of ref. 3957)

9. "Parenteral administration of 1:2:5:6-dibenzanthracene induced pulmonary tumors in mice of strains D, M, C57 brown, and C57 black, and hybrids derived from the D and C57 black strains. These strains are highly resistant to the development of spontaneous pulmonary tumors." (page 1528 of ref. 3958)

Magnus, from St. Bartholomew's Hospital, London, attempted to produce cancer of the stomach by the direct introduction of 1:2:5:6-dibenzanthracene. This was a failure except that lung tumors were produced in a high percentage of animals.

"In a series of market mice with a lung tumour incidence of from 4 to 8 per cent. multiple bronchial papillomata were produced in 95.2 per cent. by the introduction into the stomach of a suspension of 1:2:5:6-dibenzanthracene in olive oil. It is highly probable that aspiration of minute quantities of the carcinogenic agent accounts for the production of these tumours. In 75 per cent. of the affected mice the bronchial papillomata showed clear evidence of malignancy, with metastasis in two mice. The morbid anatomy of spontaneous and of artificially induced lung tumours in mice is the same. Assuming that the material introduced did in fact reach the lungs by aspiration, the smallness of the doses of 1:2:5:6-dibenzanthracene required to produce lung tumours in the mouse is emphasised." (page 30 of ref. 3955)

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The above summaries illustrate the extent of research on the most potent polycyclic aromatic hydrocarbon causing lung tumor in mice, regardless of route of administration. It should be recalled that 1:2:5:6-dibenzanthracene was not known to be present in coal tar or tobacco tar. It has remained as a laboratory research chemical substance.

Bittner from the Roscoe B. Jackson Memorial Laboratory, recorded the occurrence of spontaneous lung tumors in A stock mice and reciprocal hybrids between A and C57 black stocks. He concluded that susceptibility to spontaneous pulmonary tumors was probably transmitted by a sigle dominant Mendelian factor (3864). Breast tumor incidence was high in breeding females and low in virgin females. Diet, per se, influenced breast-tumor incidence primarily through the physical condition of mice reaching the cancer age (3549, 3959).

Lynch, from the Rockefeller Institute for Medical Research, continued with studies on tumor susceptibility and heredity. In the fifth publication of the series, she concluded:

> "A male mouse from a strain with a high incidence of spontaneous lung tumors was crossed with several females derived from a low tumor strain. The first generation of offspring were then backcrossed to individuals of the original strains. The resulting two groups of offspring differed significantly in the incidence of spontaneous tumors of the lung. These facts are discussed in relation to others previously dscovered. It seems clear from the evidence presented that there are among mice constitutional types which differ in incidence of tumors of the lung and that the differences are inherited. The number of genetic factors involved has not been determined. No influence of sex was apparent. The possibility of there being genetic factors which affect tumor age will be dealt with later." (pages 759-760 of ref. 3131)

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Experimental Carcinogenesis in Rabbits.

There were no application of polycyclic aromatic hydrocarbons to test rabbit lung. There was an abstract indicating that coal smoke over a period of 80 days diverted into a chamber caused pulmonary fibrosis but no mention of new growth (3750). Rabbits have been used for study of naphthalene metabolism, which was relevant to the induction of experimental cataract (3455). Papilloma virus was demonstrated to be transmissible from wild cotton tail rabbits to wild and domestic rabbits (3335). The intravenous injection of the virus caused malignant lesions on tarred skin (3647, 3865, 3960). It was not known whether the virus was transmitted from rabbit to rabbit in the process of tarring the ears, without intravenous injection. The carcinogenic effect of papilloma virus was discussed in a 1987 article by Harris in his P81 Exhibit, authored by Flory.

Radiation. The review article by Ewing entitled "Tissue Reactions to Radiation" related to therapeutic application rather than adverse reaction to carcinogenicity (2604). Mice with transplanted sarcoma have been useful in estimating the therapeutic dose of roentgen rays and gamma rays (3451). Full body irradiation of mice resulted in appearance of tumors including lung and breast lesions (3649). Rabbit lung has been used to demonstrate the initial hyperactivity and late death of ciliated cells following radon implantation (3650). There was no experimental basis to support or exclude the possibility that repeated chest x-ray during the 1930's or earlier was a cause of increasing incidence of lung cancer. The occurrence of malignancy in workers of luminous watch dials was well documented (3118). A similar epidemiologic study on population group exposed to chest x-ray was not conducted and reported.

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Human relevance of animal skin painting.

The skin painting studies were conducted primarily to detect carcinogenic constituents of coal tar. The therapeutic use of any agent derived from coal products had to pass a safety test. Wood demonstrated that purified mineral oil (liquid petrolatum USP) was not the cause of cancer in skin painted mice (3042, 3123). Human forms of arsenic-epithelioma and keratosis (3550) were difficult to reproduce in mice so that there were exception to the general rule of usefulness of skin painting experiments. The crucial test relating to 3:4-benzpyrene applied to human skin was conducted in 1939, prior to strict regulations of clinical testing. Cottini & Mazzone, from the University of Catania, Italy, reported their results:

> "1. Daily skin applications of a 1 per cent solution of benzpyrene in benzol in 26 human subjects for variable periods, not exceeding four months, resulted in definite manifestations localized to the treated areas. Erythema, pigmentation, desquamation, the formation of verrucae and infiltration developed in chronological order. Pigmentary and verrucous lesions were the most common observed changes. The gross and microscopic characteristics of each stage are described.
> 2. Following the suspension of treatment after a maximum of 120 applications or when evidence of infiltration appeared, the manifestations regressed completely within two to three months. Although reversible and apparently benign, the changes undoubtedly represented early stages of a process which would have ultimately gone on to neoplastic proliferation. In a broad sense they may be designated as prototypes of a precancerous process.
> 3. The alterations were more pronounced in older than in younger individuals, and on the unprotected skin surfaces. The reaction of young patients with active gummatous lesions was comparable to that observed in the older group.
> 4. In patients with pemphigus vulgaris benzpyrene produced a bullous eruption comparable in appearance and course to the spontaneous disease. The protected and unprotected skin of a patient with xeroderma pigmentosum, while extraordinarily sensitive to ultraviolet irradiation, did not react characteristically to benzpyrene.
> 5. Treatment with benzpyrene of ulcerated squamous-cell cancer of the skin was followed by temporary amelioration. In one instance an analgesic effect was observed. Limited retardation of

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> the progress of mycosis fungoides lesions in the tumor stage occurred in one case after local application of benzpyrene. Basal-cell cancer and desquamating lesions of psoriasis or porokeratosis were unaffected.
>
> 6. The assumption appears warranted that benzpyrene, if applied to human skin for protracted periods, would be carcinogenic as it is in animals." (pages 194-195 of ref. 3961)

The above conclusion applied only to skin cancer, based on human occurrence simulated by skin painting in experimental animals. However, there has been no reported human experiment of inhaling polycyclic aromatic amines to support the contention that animal exposure can be applied to human cancer. It is possible that in the annals of human experimentation conducted by Nazi physicians, carcinogens were used. This subject is discussed in Chapter IV and Part Four of this review.

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E. HOSTAL SUSCEPTIBILITY FACTORS

During the 1930's, although occupational/environmental or extrinsic factors were being investigated extensively, the intrinsic factors influencing susceptibility of host was not being overlooked. The scope of intrinsic factors included heredity, diet and nutrition, acute bronchopulmonary irritation, previous chest trauma, chronic pulmonary dust diseases, and pulmonary infections. Additionally, there were efforts to understand immunologic responses influencing ultimate new growth formation in experimental animals.

Heredity

The most significant development in strengthening the importance of inherited susceptibility was the discovery of mouse strains with lung cancer, either spontaneously or induced by coal tar skin painting (3866). The susceptibility was inherited as a dominant Mendelian gene, based on breeding and crossbreeding of two or more inbred strains (see above under Topic D, Experimental Carcinogenesis.)

According to Warthin, from the University of Michigan Hospital at Ann Arbor, it would take a detailed history of three generations of several families to show cancer proneness that was inherited (3043). He described familial predilection to cancer for the respiratory system in males, and for the breast in females. He noted several families with distinct inheritance of two organ susceptibility that was sex limited. During the 1980's, the oncogene

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responsible for lung cancer and breast cancer was reported to be in the same chromosome (see page 23).

Lung cancer in children was regarded by some experts as a form of inheritable congenital anlage that became malignant as a result of lung infection (3415, 3763). There were racial differences: Jews in New York City had higher incidence than Gentiles for lung cancer (3302), but lower incidence for cervical cancer (3456). There were differences between white and negro races in relative incidence of malignant diseases and metastasis at death (2733, 2841), but the series reported during the 1930's were limited in number to be meaningful.

The "constitutional factor in cancer" separately from the "irritational" agents that produced neoplastic growth, was announced during the 1926 International Conference on Cancer at Lake Mohawk. In an Editorial for the Bulletin for the Control of Cancer, Little re-emphasized the importance of constitutional factor which determined the tendencies towards or against the formation of cancer (3651). The susceptibility was "passed from one generation to another as part of the natural biological characteristics of the individual. If the constitutional factor was not present, there might conceivably be hyperplasia or even the formation of benign tumors, but the cancerous change would theoretically not be possible." The theory was "most promising" during the 1930's and supportive evidence became available during the next three decades.

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Diet and Nutrition

Hoffman wrote a monograph on Cancer and Diet relating to the disease in general (3701). There was no section devoted to lung cancer although relevant information was scatterred throughout the book. Hueper's unpublished study on the influence of sulfur-containing compounds were discussed on pages 271 and 641 of Hoffman's monograph. The manuscript was characterized as "the best exposition of the problem yet presented in the subject of sulfhydryl compounds."

The manuscript was later published by Hueper and two articles are appended (3311, 3449). The articles indicated that Hueper was at the Cancer Research Laboratories of the University of Pennsylvania, prior to working for the Haskell Laboratory of Industrial Toxicology at DuPont. Hueper's views on lung cancer (2623, 2933) were not discussed in Hoffman's monograph (3701) and Hoffman's article on smoking and cancer (3131).

Little wrote an Editorial on the subject of "Diet and Cancer." The relevant paragraphs on possible relationship were:

> "The experimental work which has been done with laboratory mammals has repeatedly shown that different strains of mice kept on the same diet may exhibit a widely divergent incidence of cancer. Obviously, in these cases, great differences in cancer incidence depend upon factors other than a diet which has been standardized in so far as possible.
>
> It is also well to remember that any problem of diet has several very definite phases. In the first place there is to be considered the actual amount of various food elements taken into the stomach. This is one variable. In the second place there is to be considered the physiological age and function of the various time elements in the digestive tract. This provides another variable. The third variable is the amount and rate of absorption of various food elements - a process which is the result of the interaction of the two factors already mentioned. There then follows a fourth factor, namely what the body does with the nutritive elements absorbed. The whole question of storage, metabolism, elimination of waste products and other highly involved processes enter into the situation.

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> It does not take a great deal of technical training to see how complicated the whole problem of diet actually is. To prove a direct and simple relationship between any element in the diet and the incidence of a malignant tumor is no easy matter. The number of carefully planned and scientifically controlled experiments in this field is surprisingly small. The amount of ill-conceived and loosely conducted investigation is discouragingly large.
>
> There is little prospect that the amount of the latter type of work can be diminished. People enjoy obtaining 'definite' results even though careful analysis reveals the inaccuracy of their findings.
>
> On the other hand, there is no reason why - with the availability of stocks of animals of known genetic constitution - steps should not be taken to establish valid evidence concerning the possible role of different dietary elements in the etiology of cancer. Such experimentation will, of necessity, be slow and tedious. (pages 9-10 of ref. 3652)

Little subsequently contributed to developing mouse strains necessary for meaningful carcinogenesis experiments, an accomplishment that can be regarded as largely an American contribution at a time when European and Latin-American scientists were already satisfied with their own experimental animals. Passey and his collaborators demonstrated in rats that vitamin A caused bronchial metaplasia (3644).

Acute Bronchopulmonary Irritation

The concept that bronchogenic carcinoma was preceded by pathologic or excessive regeneration as a result of acute injury to the airways originated from histopathologic studies. Bogen was among the earliest American investigator who characterized tobacco smoke as an "irritant" (3653). Fried popularized the concept (2935) and other physicians interested on lung cancer endorsed the importance of acute irritation (3013, 3235, 3531). The concentration of a chemical irritant must be low enough to exert cellular death with minimal effect on surrounding tissue to permit cellular regeneration. In cancer-prone

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individuals, regeneration was excessive, unlike an individual without the constitutional predisposition. Peller (3756) proposed a theory that irritation by cancer provoking agents led not only to a changed incidence of cancer in the irritated spot, but also to opposite changes in some of the other organs to which they have no relation. He could detect antagonism between cancer incidence between the skin and upper alimentary tract. A similar influence between skin and respiratory system has not been detected nor excluded.

Previous Chest Trauma

Ewing wrote a review article entitled "The Modern Attitude Toward Traumatic Cancer" which contained a section on lung cancer (3511). The appearance was five years prior to the revision of his monograph (4001). The difference was that the review article did not mention tobacco smoke even though Roffo had already published the results of tobacco tar on rabbit skin (see above Topic D). The possibility that Ewing hurriedly added Roffo's observation to page proofs was discussed (page 253). Ewing rejected cases with a record of previous trauma followed by lung cancer, including those cited by Adler (1201). Ewing accepted only one case reported in 1903 by Levine as traumatic in origin. Ewing could not comment on a contemporary report by Jaffe in a cancer patient who had a bullet embedded in the lung (3516). Fried, like Ewing was "sceptical of any etiologic relationship between single traumatic insults and cancer of the viscera" (3201). On the other hand, Behan wrote a monograph on Relation of Trauma to New Growths which was less critical of traumatic etiology of cancer (3901).

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Chronic Dust Diseases of Lungs

The fundamental question during the 1930's was whether exposure to occupational dust caused lung cancer. There was no question that fibrotic reactions resulted from inhalation of free silica or quartz (silicosis), coal dust (pneumoconiosis) and asbestos fibers (asbestosis). One proposed theory stated that inhaled dust was not a direct carcinogen but the tissue response in turn led to new growth, provided the individual had the "constitutional" factor of predisposition (3552, 3751, 3752, 3753). There was no information on smoking habits of workers who developed chronic lung diseases. The case reports of lung cancer patients exposed to occupational dusts and with known smoking habits are tabulated above under Topic B (page 180).

Radium miners. Since the turn of the century, miners in Joachimstal, Czechoslovakia, have had a high percentage of malignancies (53 percent) among their deaths. There was a considerable increase cancer mortality rate due to "an enormous frequency of pulmonary cancers in the age period of 35 to 54; an exceptionally high proportion of primary lung cancers, a reduced incidence of cancer in non-respiratory organs; an increased mortality from cancers other than cancer in the younger age groups (3962). It was the conclusion of Pirchan & Sikl (3236) and of Peller (3962) that the lung cancer was caused by radium emanation contained in the air of Joachimstal pits. Ventilation had reduced the radon concentration but there was no immediate reduction in lung cancer incidence because of long latent period of 10 to 20 years (3764).

Miners with silicosis. The coverage on silicosis in Ewing's monograph (4001) illustrated his tendency to favor one group and ignore conflicting opinions. As stated earlier, Ewing did not conduct any original research on

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lung cancer, and contents of his monograph represented his favored hypothesis derived from the literature. He favored the concept that "silicosis exhibits no definite tendency to produce cancer in the lung", favoring Lanza (3806), Lynch & Smith (3555), Vorwald & Karr (3869). There were anonymous articles (3817, 3828), and other signed articles (3336, 3759) that excluded or omitted the possibility that silicosis was a probable cause of cancer. On the other hand there were publications from Pennsylvania (3452, 3722), New Jersey (3529), Canada (3237, 3963) and England (3336, 3436, 3832, 3965) that endorsed the concept that silica caused carcinoma. Any influence of miners, mining company and government agencies on the medical publications has been difficult to prove or disprove. It has been difficult to obtain workers' compensation for lung cancer although the federal law permitted compensation for pneumoconiosis in the 1970's.

Asbestosis. Harris cited Lynch and Smith's article entitled "Pulmonary Asbestosis" in his written reply to the question: "Are there any of these diseases for the period covered by your report that was more evidence of an association of cigarette smoking than in the case of lung cancer?" (page 50, ERR). There was no mention of smoking in the cited article of Lynch & Smith (3555) nor in a later article by the same authors (3964). They were among early investigators who reported that some asbestosis patients, because of irritation and metaplasia, may also develop lung carcinoma.

The above authors were from the Medical College of South Carolina. Two other pathologists reported case reports of asbestosis with lung carcinoma: Egbert & Geigen from Yale University School of Medicine (3638), and Gloyne from London Hospital for Diseases of the Heart and Lungs (3238, 3556, 3641). There

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was no information on cigarette smoking habits. Most European physicians raised the possibility that asbestos fiber was the carcinogenic agent.

Pulmonary Tuberculosis

Although Ewing stated in his earlier monograph that tuberculosis was a significant etiologic factor in bronchogenic carcinoma (2801), other investigators continued to discuss case reports with both diseases. The only available article on the subject of tobacco causing tuberculosis was by Bogen from Olive View, California (3754) and this was cited by Harris in support of his statement that "although at one time tobacco was ascribed a role in the causation of tuberculosis, such an hypothesis was not seriously enterntained by the late 1930s" (SOA 7.9). Bogen's article had no references and raised questions that remained unanswered because of the advent of chemotherapy.

Fried, another monographer, expressed his opinion that was contrary to that of Ewing's. He reported 13 cases of combined tuberculosis and lung carcinoma. He proposed that the process of "cancerization" of a cavity was analogous to "epithelization" of tuberculous cavity (3547, 3551). Similar case reports were published from clinicians in New York (3021, 3620) and other Northeastern States (3325, 3615, 3829), Midwestern States (1919), and England (2530, 3337). Tuberculosis has been reported to occur with silicosis so that differential diagnosis of the superimposed bronchogenic carcinoma became complex (3457).

Hueper reviewed the controversies whether cancer favored the development of tuberculosis, or vice versa, or antagonism between both. After recounting the literature, he concluded that "the doctrine of antagonism between active

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tuberculosis and cancer is supported by numerous and reliable experimental and statistical data and pros by far more evidence in its favor than any other conception of this matter" (3045). Since Hueper is my personal choice for a posthumous expert witness, I favor his opinion instead of Ewing, Fried, and Bogen.

Several case reports were published indicating that influenza preceded the appearance of lung cancer. Since a causal relationship was disproven three decades later, a further discussion of influenza as a predisposing disease is dropped during the next two decades.

Environmental and Hostal Interactions

Hueper and other investigators reported results of animal experiments that related to interactions between carcinogenic substance and the hostal responses leading to new growth in general. Hueper compared allergic and neoplastic disorders and introduced the concept that urinary bladder tumor formation was a form of chemical allergy, and that tumor-bearing animals showed vasclo-connective tissue changes following injection of bacterial Schwartzman active substances (3639). Hueper also described immunologic aspects of leukemia (3231, 3448).

The immunological aspects of heterologous transplantation of human and other mamallian tumors were reported by Greene (3854). Decades later, the introduction of drugs with immuno-suppressive and anti-tumor effects was possible as an indirect outcome of these developments in the laboratory.

Several studies were described relating to cellular responses of lung tissue that directly or indirectly led to new growth: influenza virus in mice

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(3755), subcutaneous injections of asbestos fibers in rabbits (3046), intrapleural injections of electrolytes in rabbits (2842, 3044), vitamin A deficienty in rat (3644), inhalation of silicon carbide dust in guinea pigs (2843, 2844), intratracheal injection of silica in rabbits (3239, 3757, 3758), and metabolism of polycyclic aromatic hydrocarbons in rabbits (3455) and dogs (3554, 3760). Although human observations suggested that dyspituitarism was the probable cause of clubbing of fingers in patients with lung cancer (3240), the syndrome could not be reproduced in experimental animals.

The influence of trauma on initiation of tumor and on site of metastases were studied in experimental animals (1414, 2956). By reducing oxygen content of blood, inhalation of carbon monoxde caused a marked retardation on rate of growth of mouse carcinoma (3241). Kreyberg described dietary influences on mice with tar skin cancer (3858) and additional details are reported in the next chapter (IV).

In later decades, the subject of environment-host interactions was extensively studied. It was a subject that appealed for a cooperative effort among clinicians, biologists, chemists, biochemists, experimental pathologists, immunologists and epidemiologists. I have selected progress in environment-host interaction research as the connecting link among chapters.

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F. THEORIES OF PULMONARY CARCINOGENESIS

The theories of causation of cancer during the 1930's are essentially an extention of those discussed in earlier decades (see Chapter I and Chapter II). There is additional support for tobacco smoking, occupational/environmental factors and hostal susceptibility. The similarities and differences between the two extrinsic groups (tobacco smoking and occupational/environmental factors) are summarized below. This is followed be revisions in Harris' summary statements that continue through Chapter IV, thus completing the literature review prior to 1950. The literature for the 1940's is entitled "The Postwar Publication Explosion on Pulmonary Carcinogenesis" which was selected after collection and grouping of copies of literature. Since the entire literature before 1950 and 1950 to 1966 exceed 3000 articles that relate to pulmonary carcinogenesis, the development of a subject index has been attempted repeatedly for the past six months. The final product called Etiologic Topical Index has been tested and applied to over 600 bibliographic references for the 1930's.

Similarities and Differences Between Tobacco Smoking and Occupational/ Environmental Factors.

By reviewing the literature decade by decade, it has become apparent that by the end of the 1930's, occupational/environmental factors were more widely accepted than tobacco smoking as the extrinsic "irritant" leading to lung cancer. The emphasis in the selection of literature was to illustrate Harris'

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shortcoming such as omission of additional references by the same authors, overlooking the considerable amount of human and experimental animal studies relating to occupational/environmental causes of lung cancer, and assuming that European, Japanese and Latin American research studies on tobacco smoking were credible enough to American scientists who could not ignore the political events between the first and second World Wars. The highlights of similarities and differences between tobacco smoking and occupational/environmental factors are separated according to subtopic headings: lung cancer monographers; lung cancer morbidity and mortality; and experimental carcinogenesis.

Lung cancer monographers. Over twenty monographers devoted to human lung cancer were overlooked by Harris who favored Ewing's monograph on all forms of neoplastic diseases. The contents of twenty monographs are compared and I have concluded that there was more detailed discussion on etiology in lung cancer monographs compared to the book by Ewing. All monographers agreed that occupational/environmental factors were generally accepted as the extrinsic "irritant" on the susceptible host. The coverage on tobacco smoking was limited in scope or even omitted in half of lung monographs and review articles. The quotations on the origin of "extrinsic" hypotheses are purposely lengthy because the 1930's marked the decade of acceptance of occupational/ environmental causes of lung cancer.

Moribidty and mortality studies. German scientists preceded other Europeans and Americans in recognizing that coal tar products and combustion emission were responsible for increasing incidence of lung cancer. I have

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anticipated the forthcoming events by pooling together the literature on worker exposure and general population exposure to ambient air pollutants, under the heading of occupational/environmental. The increase in exposure of workers and general population was not documented by chemical analysis of ambient air or samples collected from work site because analytical techniques were not yet developed other than simple combustion gases such as carbon monoxide, carbon dioxide, and nitrogen oxides. The techniques for detecting polycyclic aromatic hydrocarbons were being developed in the laboratories during the 1930's and it would take two decades for applying them to field samples.

The causal association between occupational/environmental exposure to the incidence of lung cancer was based on comparative mortality rates of occupational groups in Europe. Reports from the United States were limited to case reports collected in a hospital. There were no case control comparisons because pathologists and clinicians were not yet aware of the necessity. Furthermore, Americans were more concerned with improving antemortem diagnosis and treatment rather than searching and proving the necessity of extrinsic factors. I have the general impression that most clinicians subscribed to the importance of an inherited constitutional predisposition to irritants. Since there were several possible irritants, and predisposition could not be corrected, the only resort was early diagnosis for treatment.

The prevention of lung cancer by discovering that most lung cancer patients were tobacco smokers, was attractive to German and Spanish-speaking scientists numbering about a dozen. They cited each other's scientific accomplishments, including the work of three American laboratories. However, the majority of clinicians overlooked these reports, implicating that tobacco

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smoking was a cause of lung cancer which was reflected in secondary citations in the literature of the 1930's. Harris used the tobacco smoking articles, added them to those appearing in the 1940's and formulated his opinion that cigarette manufacturers should have undertaken research relating to lung cancer. But American scientists in general ignored the work of three groups in the United States, and works by German-speaking, Spanish-speaking and Japanese-speaking scientists, probably because of the spread of Nazism, Franco's dictatorship, and Japanese imperialism.

Experimental Carcinogenesis. The most extensive contributions in the understanding of skin cancer were from England and Argentina. Roffo, from Buenos Aires, contributed to the understanding of carcinogenic effects of ultraviolet radiation on the skin. It should be emphasized that mice were used by Roffo for his study of ultraviolet light causing skin cancer. When Roffo initiated his studies on tobacco-associated cancer, he used rabbits instead of mice, and continued observing skin cancer even though lung cancer was the disease supposedly caused by tobacco smoking. His two dozen publications were ignored by most Latin Americans, North Americans and Europeans for the selection of rabbit skin for tests for carcinogenecity, and also because there has been some notoriety in his family name that continued during Peron's regime up to the second return of the Peronistas in Argentina this year. Harris noted less than ten publications that cited Roffo's work on rabbit skin, all of them accepting the applicability of skin cancer studies to lung cancer in humans.

The British laboratories initiated mouse skin painting experiments because of the occurrence of tar skin cancer in humans. The laboratories of Campbell and of Kennaway were very active in identifying carcinogenic cons-

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tituents in coal tar. There was no question that the ultimate effect was skin cancer in mice as a result of skin painting. There were also some observations that inhalation or intratracheal injection of coal tar particulates resulted in lung cancer in experimental animals. There were some reports that skin painting of coal tar resulted in lung neoplasm in mice. The conflicting results relating to experimental lung neoplasms are recounted above to serve as a background history of events after the 1930's. The following questions are addressed in the next chapter: Can skin painting experiments relate to pulmonary carcinogenesis? What is the difference in biologic effects and chemical composition of coal tar and "tobacco tar"? What is the significance of the discovery of dibenzanthracene derivative, as the most potent carcinogen, injectable or skin painted, causing lung cancer in susceptible strains of mice? Did scientists use this chemical substance, not present in coal or tobacco tar, as a model for a pulmonary carcinogen administered by dermal, pulmonal, oral, or parenteral injection? How did scientists interested in tobacco and health use this potent carcinogen, either to prove or disprove the causal association of tobacco smoking and lung cancer? I do not know the answers because some of the above questions were not raised in the course of collecting the literature that started October 1988.

Revision of Harris' State of the Art Summary Statements.

I have attempted to revise Harris' statemnts on the basis of literature he has overlooked. Summary Statements under Section 9 of his SOA report reproduced above (pages 136, 137) are revised as follows:

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9.1. During the 1930's, there was no reason for manufacturer of cigarettes to conduct or sponsor research into potentially cancer causing effects of its products. The literature on lung cancer, both on animal and human studies, overwhelmingly favored occupational/environmental irritation of susceptible host as the cause. There were a dozen articles proposing tobacco smoke as a cause but they did not meet the standards of acceptability using the model of coal tar causing human and experimental animal cancer.

9.2. The scientific research available by the late 1930's was limited to questionaire survey in three instances. Most other studies on human lung cancer were mortality comparisons of occupational groups that supported the theory that there were chemical irritants in the work environment. The techniques for analysis of components of coal tar were being developed in the 1930's, which were applied to tobacco tar during the next decade. Tobacco smoke was analyzed to the same extent as combustion products containing carbon dioxide, carbon monoxide, aldehydes and alkaloids. There were no animal models for conducting long term inhalational experiments for research on lung cancer of animals exposed to suspected human carcinogens such as dust particles containing coal dust, silica and asbestos fibers. Intratracheal injections of coal tar particles caused lung cancer in experimental animals but similar injection of "tobacco tar" was not equally successful.

9.3. Statements on cancer research support is reviewed in Chapter IV.

9.4. During the late 1930's, and through the early 1940's discussed in Chapter IV, the "scientific evidence that cigarette smoking caused cancer" was minimal and largely from German, Spanish and Japanese researchers. Since Americans were against Nazism, Franco's civil conflict in Spain, and Japanese

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imperialism, the evidence was not credible. Warning to consumers was not necessary because other consumer products (like coffee), with known cardiotixic properties, did not require labeling (see Part IV). Furthermore, consumer products that caused skin cancer (like creosote), did not carry a warning label. The human carcinogenicity of coal tar products was already known since the 18th century, and support by skin cancer in animal experiment were available since the beginning of this century.

9.5. The scientific evidence on "other potentially harmful effects of cigarette smoking" available during the 1930's and up to 1942, was not of a nature to require warning to consumers. Additional reasons are discussed in Chapter IV.

9.6 and 9.7. These are reviewed in Chapter IV.

Guidance Needed For Remainder of Project.

I need advise on how detailed or shortened the remaining Chapters should be. The quotations in this Chapter devoted to the 1930's are intentionally lengthy because these articles, widely quoted during the next three decades, and by Harris, are in foreign languages. Furthermore, the conflicts were largely between authorities expressing opinions, counter-opinions and cross-opinions. Most opinions were interpretations of facts that were more abundant for occupational/environmental factors than for tobacco smoking.

I am aware that until the 1980's, there is "no positive proof that cigarette smoking is the most significant cause of lung cancer." The literature prior to 1950 is abundant on occupational/environmental factors, more so than tobacco smoking but the situation was slowly reversed between 1950 and 1966.

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Am I to continue to follow all important hypothesis in addition to tobacco smoking, such as: occupational/environmental exposure to fossil fuel products, combustion emission, industrial emission, dust emitted during mining, farming, and indoor occupations; and factors influencing hostal susceptibility such as heredity, constitutional hypothesis, diet and nutrition, previous chest trauma, pulmonary infections and chronic dust diseases of the lung? Am I to concentrate only on statements that are still valid after 1966 and ignore those that were proven to be untrue after 1966 because of availability of new research studies? Shall I stop using lengthy quotations and follow Harris' style of selected sentences to support summary statements? Shall I substitute the use of an Etiologic Topical Index, or a further improvement of it, and simply present articles in a logical sequence of gradation of importance?

A prompt answer to the above questions will be appreciated for work on this project will be put into low gear until such answers are received. I might remind Ms. Thompson and her associates that the scope of this review has not been covered in any monograph published before or since 1966.

Etiologic Topical Index.

While examining the more than 600 articles for this chapter, the necessity to formulate an etiologic topical code became urgent. The overwhelming purpose of the literature search is to compare the role of (a) tobacco smoking, (b) occupational/environmental factors, and (c) hostal susceptibility factors, with special reference to their interactions in pulmonary carcinogenesis. The topical code must also signify the source of information, such as literature review, human studies, and animal studies. It is also

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essential that the topical code should be simple enough to determine whether the article supports the tobacco smoking hypothesis, or other causes of lung cancer.

With our limited computer facility, indexing by word was out of the question; instead, an alpha numerical system evolved consisting of a letter followed by a three digits starting with A111 to Z999 and 000 to mean no etiologic information. Alpha (A to Z) represents the general form and subject of the publication. Alpha is followed by a numeric three-digit as information rating: 2nd position _0__ for tobacco smoking; 3rd position __0_ for occupational/environmental; and 4th position for ___0 for hostal susceptibility. Numeric 0 means no information; levels 1 to 4 mean various levels of support for the tobacco smoking hypothesis but against occupational/ environmental and hostal susceptibility; and level 5 means available informa- tion does not permit a lower or higher rating but will be altered at a later date; levels 6 to 9 mean that the article contains information that is <u>against</u> tobacco smoking hypothesis and that occupational/environmental factors and hostal susceptibility are the <u>more important etiologic factors</u>. Publications with ratings of 1 to 4 for all three positions contain information supporting claims of Harris and plaintiffs that cigarette smoking is a significant cause of lung cancer, and its etiologic role is <u>more important</u> than occupational/environmental factors and hostal susceptibility. On the other hand, publications with ratings of 6 to 9 contain information helpful to the tobacco industry, that tobacco smoking as a cause of lung cancer has not been proven to the extent that known pulmonary carcinogens (dibenzanthracene derivatives BCME, creosote) have been positively demonostrated. Such a statement is unlikely to appear

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in the open literature but the published information suggest the relative importance of tobacco smoking compared to occupational/environmental factors and hostal susceptibility. Rating 6 to 9 signify that tobacco smoking is not as important as occupational/environmental and hostal susceptibility.

The three numbers should be regarded as relative ratings of tobacco smoking compared to non-tobacco etiologic factors. The specific meaning of the alpha numeric symbols is as follows:

Form and Subject:

Tobacco constituents and lung cancer

- A___ Animal inhalation and intratracheal injection
- B___ Biologic effects other than specific procedures (A, C to F)
- C___ Chemistry of tobacco leaf, tobacco smoke and cigarette manufacture
- D___ Dermal and oral injection of tobacco tar (animal)
- E___ Coal tar and constituents: skin, oral, injection (animal)
- F___ In vitro testing
- G___ Case reports
- H___ Case reports with controls; retrospective
- I___ Prospective studies
- J___ Morbidity studies; other forms of smoking associated diseases
- K___ Mortality studies; other forms of cancer

Occupational/environmental: animal and human studies.

- L___ Coal tar products (except animals under E)
- M___ Vehicular emissions
- N___ Occupation exposure
- O___ Industrial emissions (air, water, food, contaminants)
- P___ Polycyclic aromatic hydrocarbons
- Q___ Suspected carcinogens (radiation, metals, nitrosamines)

Hostal Predisposition

- R___ Heredity (constitutional hypothesis, animal breeding)
- S___ Diet and nutrition
- T___ Pre-existing diseases (tuberculosis, viral, trauma)
- U___ Dust diseases
- V___ Host-environment-tumorinteractions

Special Publications

- W___ Bibliography, Congressional Hearing, Special Society Report
- X___ "Reserved"
- Y___ Editorial, Letter to Editor, news items
- Z___ Monograph, review article, symposium

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Numerical Ratings

Tobacco Smoking (TS)	Occupatioal/ Environmental (OE)	Host Susceptibility (HS)
1 = overall TS > OE, HS	1 = overall OE < TS	1 = overall HS < TS
2 = human TS > OE, HS	2 = human OE < TS	2 = human HS < TS
3 = animal TS > OE, HS	3 = animal OE < TS	3 = animal HS < TS
4 = opinion TS > OE, HS	4 = opinion OE < TS	4 = opinion HS < TS
5 = Uncertain	5 = Uncertain	5 = Uncertain
6 = opinion TS < OE, HS	6 = opinion OE > TS	6 = opinion HS > TS
7 = animal TS < OE, HS	7 = animal OE > TS	7 = animal HS > TS
8 = human TS < OE, HS	8 = human OE > TS	8 = human HS > TS
9 = overall TS < OE, HS	9 = overall OE > TS	9 = overall HS > TS
0 = no information	0 = no information	0 = no information

Examples of the rating system:
111 = tobacco smoking is significant, or more important, cause of lung cancer than occupational/environmental factors and hostal susceptibility.
999 = tobacco smoking is not, or less important, than occupational/ environmental and hostal susceptibility

Application of Topical Index. The above alpha numeric system of indexing is being applied to the literature of the 1930's. Theoretically, there are 25 alphabetical topics (X is reserved) and 1000 ratings for published information, a total of 25000 possible combinations of this alpha numeric system. The rating number must be used with the title of publication and authors because details of animal species, statistical analysis, population groups, chemical procedures, experimental protocol, are not included in the alpha numeric indexing system. The system will serve only one purpose: to identify articles that support the position that tobacco smoking is not, or is not as important cause of lung cancer, compared to occupational/environmental and hostal susceptibility factors, and vice versa. The application of Etiologic Topical Index to Harris' selected scientific articles and to articles that I have collected will be forwarded upon receipt of a new computer promised by mid-June, and the subsequent programing and entry of data in it.

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BIBLIOGRAPHY

PART TWO: CHAPTER III - THE 1930's

Note: The four-digit numerical system was described in the Bibliography of Part One (page 18). The 3000 series include publications from 1930 to 1939: thus, 3000's were published in 1930, 3100's in 1931, 3200's in 1932, 3300's in 1933, and so on until 3900's in 1939. Symbols used on cited publications are as follows:

DTH = Deposition Transcript Harris; exhibit and pages
ERR = Expert's Response to Requests (for additional information)
TOP = Transcript of Proceedings; exhibit and pages
SOA = Harris' State of the Art
P = Secondary citations in Harris' representative key articles
DMA = Citations in my 1986 Critique to replace mislaid copies
WHM = Articles derived from 1967 Wynder & Hoffman Monograph
SGR = Cancer references in the 1964 Surgeon General's Report
[] = Harris' SOA report, DTH exhibits, and ERR
# = Articles forwarded with earlier chapters (see Cumulative Index)
* = Articles to be submited with later chapters or at end of project
+ = Foreign articles in need of English translation

Entries without brackets "[]" were derived from manual searches of medical indices as explained on page 11.

Color code of slips attached to photocopies:

Blue = Harris' citations
Orange = Hueper's publications
Green = Wynder & Hoffman's references
Cream = Secondary references in Harris' "P" exhibits; SGR references
Yellow = Tobacco monograph references
White = Index Medicus
Buff = ID numbers from New York collection
Pink = IARC references

1901 to 1929 Monographs and Periodicals

0941 Adler I: Remarks on primary endothelioma of lung and pleura, with demonstrations. J Med Res 7: 175-186, 1901.

0943# Musser JH: Primary cancer of the lung. Trans Assoc Am Phys 18: 625-636, 1903.

0945# Packard M: Case of primary malignant tumor of the lung. Med News NY 86: 303-304, 1905.

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Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

0956 Adler I: Preliminary note on some effects of tobacco on the tissues of rabbits. J Med Res 8: 309-315, 1902.

0957 Adler I, Hensel O: Intravenous injections of nicotine and their effects upon the aorta of rabbits. J Med Res 15: 229-240, 1906.

0958 Musser JH: Primary cancer of the lung. U Penn Med Bull 289-296, 1903.

0959 Jacobi A: Carcinoma of the right lung. A clinical lecture. Med Gaz 392-393, 1883.

1101+ Wacker L, Schmincke A: Experimentelle Untersuchungen zur kausalen Genese atypischer Epithelwucherungen. Munch Med Wochenschr 58:1607-1613, 1680-1682, 1911.

1201# Adler I: Primary malignant growths of the lungs and bronchi. New York: Longmans, Green, and Co. vii-xii, 3-311, 1912. [Cited P6, P90, P145, P161, P189, P214, P278, P289, P379]

1414 Jones FS, Rous P: On the cause of the localization of secondary tumors at points of injury. J Exp Med 20: 404-415, 1914.

1513+ Yamagiwa K, Ichikawa K: Experimentelle Studie uber die Pathogenese der Epithelialgeschwulste. Mitteilungen aus der Medizinischen Fakultat der Kaiserlichen Universitat zu Tokyo 15: 235-344, 1915.

1611# Scott E, Forman J: Primary carcinoma of the lungs. Med Rec 90: 452-455, 1916.

1711# Packard M: Primary malignant neoplasm of the lung. Am J Med Sci 154: 351-365, 1917. [DMA 503]

1811# Packard M: Primary malignant neoplasms of the lung and pleura. NY J Med 18: 472-478, 1918. [DMA 504]

1814# Yamagiwa K, Ichikawa K: Experimental study of the pathogenesis of carcinoma. J Cancer Res 3: 1-21, 1918.

1919 Hedblom CA: Pulmonary suppuration. Med Rec 96: 441-453, 1919. [Cited P189]

2001# Winternitz MC, Wason IM, McNamara FP: The pathology of influenza. New Haven: Yale University Press, 39-61, 1920. [Cited P6, P180, P181, P214; SGR 371; WHM 249]

2117# Friedman GA: Carcinoma of the lung, report of a case. Med Rec 100: 980-981, 1921.

2215# Dana HW, McIntosh R: Obstruction of superior vena cava by primary carcinoma of lung, pathological report. Am J Med Sc 163: 411-425, 1922.

2062855415

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

2221# Leitch A: Paraffin cancer and its experimental production. Br Med J 2: 1104-1106, 1922. [SGR 203; DMA 622]

2319# Folson SA: A case of primary carcinoma of the lung. J Med Assoc Georgia 12: 406-412, 1923.

2321# Kimura N: Artificial production of a cancer in the lungs following the intrabronchial insufflation of coal tar. Jpn Med World 3: 45-47, 1923. [Cited P131, P181]

2322# Leitch A: The experimental injury into the causes of cancer. Br Med J 2: 1-7, 1923. [DMA 409]

2328+ Hampeln P: Haufigkeit und Urasache des primaren Lungenkarzinoms. Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie. 36: 145-150, 1923.

2329+ Schmorl: Uber den Schneeberger Lungenkrebs. Ver Dtsch Ges Pathol 10: 192196, 1923.

2330+ Oberndorfer S: Das Lungenkarzionom. Munch Med Wochenschr 18: 688-692, 1923.

2415# Kennaway EL: On cancer-producing tars and tar-fractions. J Ind Hyg 5: 462-488, 1924. [Cited P45, P129, P264]

2416# Kennaway EL: The formation of a cancer-producing substance from isoprene (2-methyl-butadiene). J Pathol Bacteriol 27: 233-238, 1924. [Cited P129, P264; WHM 145, etc.]

2421+ Seyfarth C: Lungenkarzinome in Leipzig. Dtsch Med Wochenschr 50: 1437-1499, 1924.

2422+ Assmann H: Zur Frage der Pathogenese und zur Klinik des Bronchialkarzinomas. Med Klin Wochenschr 50: 1757-1760, 1924.

2423+ Möller P: Carcinome pulmonaire primare chez les rats pie badigeonnes au goudron. Acta Pathol Microbiol scand 1: 412-437, 1924.

2517# Kennaway EL: Experiments on cancer-producing substances. Br Med J 2: 1-4, 1925. [SOA P129; Cited P81]

2520# Murphy JB, Sturm E: Primary lung tumors in mice following the cutaneous application of coal tar. J Exp Med 42: 693-700, 1925. [Cited P38, P39, P131, P158, P181; SGR 251; WHM 382]

2524# Kennaway EL: The anatomical distribution of the occupational cancers. J Ind Hyg 7: 69-93, 1925.

2526+ Staehelin R: Uber die Zunahme des primaren Lungenkregses. Klin Wochenschr 4: 1853-1858, 1925.

2062855416

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

2527+ Kikuth W: Uber Lungencarcinom. Virchows Arch Pathol Anat 255: 107-128, 1925.

2528+ Heilmann P: Uber die Zunahme des primaren Lungencarcinoms vom Standpunkte der Hygiene aus betrachtet. Virchows Arch Pathol Anat 255: 549-554, 1925.

2529+ Berblinger W: Zie Zunahme des primaren Lungenkrebses in den Jahren 1920-1924. Klin Wochenschr 4: 913-916, 1925.

2530 Lakin CE: Specimen of carcinoma of lung arising in a tuberculous cavity. Trans Med Soc London 49: 73-43, 1925.

2531 Dublin LI, Fisk EL, Kopf EW: Physical defects as revealed by periodic health examinations. Am J Med Sci 170: 576-594, 1925. [Cited P152]

2604 Ewing J: Tissue reactions to radiation. Caldwell lecture, 1925. Am J Roentgenol 5: 93-115, 1926.

2615# Perry MW: Primary carcinoma of the lung. Int Clin 3: 194-200, 1926.

2622# Bel GS: Primary carcinoma of the lung. Med Clin NA 4: 887-893, 1923. [Cited P189]

2623# Hueper W: Primary gelatinous cylindrical cell carcinoma of the lungs. Am J Pathol 2: 81-90, 1926. [Cited P181]

2629 Cave HW: Primary carcinoma of the lung. Am J Surg 40: 141-146, 1926.

2630 Barnard WG: The nature of the "oat-celled sarcoma" of the mediastinum. J Pathol Bacteriol 29: 241-244, 1926. [Cited P6]

2711# Perret JM: Primary intra-thoracic malignancy. New Orleans Med Surg J 80: 213-228, 1927. [SOA 189, key P189, DTH exhibit 84, Cited P145]

2719# Tylecote FE: Cancer of the lung. Lancet 2: 256-257, 1927. [SOA 189, key P271, DTH exhibit 85; cited P90, P115, P181, P289]

2720# Helwig FC: Influence of tobacco and other extracts on the epithelial cell. J Kansas Med Soc 27: 37-40, 1927. (Cited P159, P398; DMA 411]

2721# Duguid JB: The incidence of intrathoracic tumours in Manchester. Lancet 2: 111-125, 1927, [Cited P115, P181, P271]

2722# Klotz O: Cancer of the lung; with a report upon twenty-four cases. Can Med Assoc J 17: 989-996, 1927. [Cited P181]

2730* Lombard H, Doering CR: Cancer in Massachusetts. 1. The relationship between cancer and density of population in Massachusetts. Proc Nat Acad Sci 13: 728-735, 1927.

2062855417

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

2731+ Katz K: Statistischer Beitrag zur Kenntnis des Lungencarcinoms nach dem Sektionsmaterial des Heidelberger Pathologischen Instituts. Z Krebsforsch 25: 368-380, 1927.

2732+ Probst R: Die Haufgkeit des Lungencarcinoms. Statistische Untersuchungen am Material des path. Institutes der Universitat Zurich. Z Krebsforsch 25: 431-453, 1927.

2733* Pearl R, Bacon AL: Biometrical studies in Pathology. V. The racial and age incidence of cancer and of other malignant tumors. Arch Pathol Lab Med 3: 963-992, 1927.

2801# Ewing J: Neoplastic diseases - a treatise on tumors. Third Edition. Philadelphia: WB Saunders Co., pages 851-863, 1082; 1928.

2802+ Huguenin R: Le cancer primitif du poumon; etude anatomo-clinique. Paris: Masson y Cie, 330 pages, 1928. [Cited P181]

2814# Stivelman BP: The roentgen ray in the diagnosis of primary pulmonary neoplasm. JAMA 91: 1690-1694, 1928. [Cited P181]

2824# Henry SA: Mule spinners' cancer: the time necessary for its production. J Hyg 28: 100-103, 1928. [Cited P131]

2825# Kennaway EL, Sampson B: Tumours of the skin and mammary gland caused by pyrogenous products of cholesterol. J Pathol Bacteriol 31: 609-612, 1928. [SOA 133; Cited P81]

2826# Smith RE: The etiology of primary lung carcinoma: an experimental and clinical investigation. J Cancer Res 12: 134-142, 1928. [Cited P164, P181]

2827# Helwig FC: The growth=producing effects of extracts of tobacco on mice. JAMA 91: 150-152, 1928. [Cited P81, P244, P245, P264, P291; WHM 256; DMA 412]

2833* Lombard HL, Doering CR: Cancer studies in Massachusetts. 2. Habits, characteristics and environment of individuals with and without cancer. N Engl J Med 198: 481-487, 1928. [SOA 152, key P152, DTH Exhibit 34, TOP 1539-1543; Cited P208; SGR 221]

2839* Bigelow GH: Experience with the program of cancer control in Massachusetts. Am J Pub Health 18: 413-420, 1928. (Cited P152]

2841* Pearl R, Bacon AL: Biometrical studies in Pathology. VI. The primary site of cancers and of other malignant tumors. Arch Pathol 6: 67-89, 1928.

2842 Young JS: Experimental production of metaplasia and hyperplasia in the serosal endothelium, and of hyperplasia in the alveolar epithelium of the lung of the rabbit. J Pathol Bacteriol 31: 265-275, 1928.

2062855418

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

2843 Willis HS: The pulmonary effect of over three years' exposure of guinea pigs to silica dust. Am Rev Tuberc 17: 253-267, 1928.

2844 Willis HS, Brutsaert P: Tumor-like structures in the lungs of guinea pigs artificially exposed to silica dust. Am Rev Tuberc 17: 268-278, 1928.

2845 Bonser GM: The incidence of tumours of the respiratory tract in Leeds. J Hyg 28: 340-354, 1928.

2911# Hoffman FL: Cancer of the lungs. Am Rev Tuberc 19: 392-406, 1929. [SOA 115, key P115; Cited P90, P181, P289]

2925# Hunt TC: Pulmonary neoplasms - a report of twenty-six cases. Lancet 1: 759-762, 1929.

2927# Simpson SL: Primary carcinoma of the lung. Q J Med 22: 413-449, 1929. [Cited P181,P334]

2928# Bogen E: The composition of cigarets and cigaret smoke. JAMA 93: 1110-1114, 1929. [SOA 25; key P25; Cited P26, P28, P74, P116, P159, P398]

2931# Lickint F: Tabak und Tabakrauch als atiologischer Faktor des Carcinoms. Z Krebsforsch 30: 349-365, 1929. [SOA 145, key P145; Cited P28, P81, P116, P181]

2933# Hueper WC: Carcinoma of the lung. Illinois Med J 56: 296-304, 1929.

2935 Fried BM: Primary carcinoma of the lungs. III. Histogenesis and metaplasia of bronchial epithelium. Arch Pathol 8: 46-67, 1929.

2951 Lombard HL, Doering CR: Cancer studies in Massachusetts. 3. Cancer mortality in nativity groups. J Prev Med 3: 343-361, 1929.

2955+ Konrad A, Franke W: Uber primare Lungenkarzinome. Dtsch Med Wochenschr 55: 652-564, 1929.

2956 Knox LC: Trauma and tumors. Arch Pathol 7: 274-311, 1929.

1930 Monographs and Reviews

3001 Cabot RC: Physical Diagnosis. New York: William Wood & Co., 339-348, 1930.

3002 Emerson CP: New growths in the lung. In: A Text-book of Medicine, RL Cecil, Editor. Philadelphia: WB Saunders Co., 865-867, 1930.

2062855419

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3003 Davidson M: Cancer of the Lung and Other Intrathoracic Tumours. Bristol: John Wright & Sons Ltd., 1-173, 1930. [Cited P58]

1930 Periodicals

3011 Bonner LM: Primary lung tumor. Report of six cases with necropsies. JAMA 94: 1044-1049, 1930. [Cited P181]

3012 Wells HG, Cannon PR: Primary carcinoma of the lung following trauma. Tr Chicago Pathol Soc 13: 187-191, 1930; Arch Pathol 9: 869-873, 1930. [Cited P181, P334]

3013 Fremont-Smith M, Lerman J, Rosahn PD: Primary carcinoma of the lung. A study of 18 autopsied cases. N Engl J Med 203: 473-477, 1930. [DMA 525]

3014 Lord FT, Mallory TB: Cabot Case Records, Case 16161 - An intrathoracic diagnostic problem presenting unusual clinical aspects. N Engl J Med 202: 779-781, 1930.

3015 Thomas GW, Mallory TB, White PD: Cabot Case Records, Case No. 16331 - An unusual combination of dyspnea, cyanosis, clubbing of the fingers, back pain, paralysis below the waist and water-hammer pulsation of the pulmonary artery. N Engl J Med 203: 330-332, 1930.

3016 Wittich FW: Case reports. Lancet 50: 508-509, 1930.

3017 Colton WA: Primary carcinoma of the lung. US Vet Bur Med Bull 6: 1002-1004, 1930.

3018 Rabinovitch J, Harms FL: Primary carcinoma of the lung, with report of a case. J Missouri Med Assoc 27: 381-384, 1930.

3019 Miller JA, Jones OR: Primary carcinoma of the lung. Am Rev Tuberc 21: 1-55, 1930.

3020 Rosahn PD: The incidence of primary carcinoma of the lung. Am J Med Sc 179: 803-811, 1930. [DMA 532; Cited P6, P181, P278, P334]

3021 Von Glahn WC: Neoplasms of the Lung. Am Rev Tuberc 21: 57-69, 1930. [Cited P181]

3022 Torek F: Removal of metastatic carcinoma of the lung and mediastinum. Suggestions as to technic. Arch Surg 21: 1416-1424, 1930.

3023 Karsner HT, Saphir O: Small cell carcinomas of the lung. Am J Pathol 6: 553-561, 1930. [Cited P163]

3024 Funk EH: The clinical manifestations of primary bronchial carcinoma. JAMA 95: 1879-1882, 1930. [Cited P181]

2062855420

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3025 Paterson R: The relationship between the clinical and pathological findings in primary pulmonary malignancy. Can Med Assoc J 22: 333-337, 1930. [Cited P181]

3026 Boyd W: Notes on the pathology of primary carcinoma of the lung. Can Med Assoc J 23: 210-217, 1930. [Cited P163, P180, P181, P278]

3027 Hodge G: Primary carcinoma of the lungs and bronchi. Can Med Assoc J 22: 60-64, 1930.

3028 Jackson C: Malignant growths of the lung. Bronchoscopic diagnosis. Arch Otolaryngol 12: 747-752, 1930. [Cited P181]

3029 MacCallum WG: Carcinoma of the lung. Trans Assoc Am Physicians 45: 77-84, 1930.

3030 Goltz EV: Primary carcinoma of the lungs and bronchi. Minnesota Med 13: 605-612, 1930. [Cited P181]

3031 Mertens VE: Zigarettenrauch eine Ursache des Lungenkrebses? Z Krebsforsch 32: 82-91, 1930. [SOA 164; ERR P164; TDH Exhibit 86, 87, P683; WHM page 683, 685; Cited P28, P181]

3032 Arkin A: Bronchus carcinoma. Med Clin NA 13: 1255-1276, 1930. [Cited P6]

3033 Fried BM, Buckley RC: Primary carcinoma of the lungs. IV. Intracranial metastasis. Arch Pathol 9: 483-527, 1930. [Cited P132]

3034 Roffo AH: Leucoplasia tabaquica experimental. Bol Inst Med Exp 7: 130-144, 1930. [SOA 222; ERR P397; TDH Exhibit 50; TOP p 2048; SGR 297; Cited P81, P224, P226, P229, P231, P291]

3035* Roffo AH: Leucoplasie experimentale produite par le tabac. Rev Sud Am Med Chir 1: 321-330, 1930. [SGR 296; Cited 226]

3036 Roffo AH: Desarrolo de un carcinoma en el conejo por el tabaco. Bol Inst Med Exp 7: 501-538, 1930. [SOA 223; TOP 2048; German version appeared as Reference 3127]

3037 Maxwell J, Nicholson WA: A clinical study of bronchial carcinoma. Q J Med 24: 29-53, 1930. [Cited P181]

3038 Arai J, Kikitsu Y: On analytic and statistical studies of the cancer in the lungs. Tran Jpn Pathol Soc 20: 774-781, 1930.

3039* Kennaway EL: LVII. Further experiments on cancer-producing substances. Biochem J 24: 497-504, 1930. [Cited P 234 Roffo error; P264]

3040* Kennaway EL, Hieger I: Carcinogenic substances and their fluorescence spectra. Br Med J 1: 1044-1046, 1930. [Cited P264]

2062855421

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3041 Watson AF, Mellanby E: Tar cancer in mice: (1) The technique of the comparative experiment. Br J Exp Pathol 11: 267-281, 1930. [Cited P39].

3042 Wood FC: The noncarcinogenic nature of purified mineral oils. JAMA 94: 1641-1643, 1930.

3043 Warthin AS: Heredity of carcinoma in man. Ann Intern Med 4: 681-696, 1930. [DMA 303]

3044 Young JS: Epithelial proliferation in the lung of the rabbit, brought about by intrapleural injection of solutions of electrolytes - a physico-chemical interpretation of the phenomenon. J Pathol Bacteriol 33: 363-380, 1930.

3045 Hueper WC: Tuberculosis and cancer. Am Rev Tuberc 22: 271-285, 1930.

3046 Gloyne SR: The reaction of tissues to the asbestos fibre, with reference to pulmonary asbestosis. Tubercle 11: 151-153, 1930.

1931 Monographs and Reviews

3101 Fried BM: Primary carcinoma of the Lung. Medicine. Baltimore: Williams & Wilkins Co. 10: 373-508, 1931. [Cited P6, P181]

3102+ Giesewetter FW: Ueber das primare Lungencarcinom. Marburg: Buchdrucckerei Joh. Hamel, 32 pp, 1931.

3103+ Verga P, Botteri G: Il carcinoma primitivo del polmone (studio anatomo istologico e clinico). Bologna: L. Cappelli, 204 pp, 1931.

1931 Periodicals

3111 Carrington TS: Primary infiltrating carcinoma of the lungs. US Vet Bur Med Bull 7: 257-258, 1931.

3112 Frothingham C: The differential diagnosis between pulmonary tuberculosis and pulmonary or bronchial malignant neoplasms. Am Rev Tuberc 23: 107-119, 1931.

3113 Allen CI, Smith FJ: Primary carcinoma of the lung, with a report of a case treated by operation. Trans Am Climat Clin Assoc 47: 201-220, 1931. Surg Gynec Obst 55: 151-161, 1932.

3114 Kirklin BR, Ochsner HC: The roentgenologic study of pulmonary metastatic growths. Radiology 17: 435-448, 1931.

3115 Simons EJ: Primary carcinoma of the lungs with case report. Lancet 51: 542-547, 1931. [DMA 546]

2062855422

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3116 Polevski J: Primary carcinoma of the lungs. Pathognomonic signs in the diagnosis. Arch Intern Med 48: 1126-1137, 1931. [Cited P181]

3117 Moses HM: Malignancy in the lung: including eight primary carcinomas with autopsy findings. Ann Intern Med 5: 765-792, 1931. [DMA 533]

3118 Marland HS: The occurrence of malignancy in radioactive persons. A general review of data gathered in the study of the radium dial painters, with special reference to the occurrence of osteogenic sarcoma and the inter-relationship of certain blood diseases. Am J Cancer 15: 2435-2516, 1931.

3119 Menne FR, Bisaillon M, Robertson TD: Bronchogenic carcinoma. A pathologic and clinical study of sixteen instances. Northwest Med 30: 155-174, 1931. [Cited P163, P181]

3120 Edwards AT: Malignant disease of the lung. Br Med J 1: 129-132, 1931.

3121 Peet EW: Primary pulmonary carcinoma: with special reference to its increased incidence in the area of Newcastle-upon-Tyne. Newcastle Med J 11: 97-106, 1931. [Cited P181]

3122 Sharp GS: The diagnosis of primary carcinoma of the lung by aspiration. Am J Cancer 15: 863-870, 1931. [Cited P180, P181]

3123 Wood FC: The non-carcinogenic nature of purified mineral oils. Am J Cancer 15: 319, 1931.

3124 Berblinger W: Zunahme des Lungenkrebses und Staublungenerkrankung. Med Klin (Berlin) 11: 1337-1342, 1931.

3125 Lynch CJ: Studies on the relation between tumor susceptibility and heredity. V. The influence of heredity upon the incidence of lung tumors in mice. J Exp Med 54: 747-760, 1931.

3126 Roffo AH: El tobaco en el cancer de vejiga. Bol Inst Med Exp 8: 277-324, 1931.

3127 Roffo AH: Durch Tabak beim Kaninchen entwickeltes Carcinom. Z Krebsforsch 33: 321-332, 1931. [SOA 224; ERR P224; DTH Exhbit 54, 55; TOP 2048; Cited P28, P81, P159 same as P398; P235, P264, P291; German version of Reference 3036]

3128 Henry SA, Kennaway NM, Kennaway EL: The incidence of cancer of the bladder and prostate in certain occupations. J Hyg (Lond) 31: 125-137, 1931. [Cited P131]

3129+ Chikamatsu T: I. Kunstliche Erzegung der Krebses durch Tabakteer bei Kaninchen und Maus. Trans Jpn Pathol Soc 21: 244-247, 1931.

2062855423

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3130 Twort CC, Twort JM: The carcinogenic potency of mineral oils. J Ind Hyg 13: 204-226, 1931. [SGR 348]

3131 Hoffman FL: Cancer and smoking habits. Ann Surg 93: 50-67, 1931. [SOA 116; key P116; TDH Exhibit 36 page 239; Cited P28, P81, P244, P398, P159; WHM 246]

1932 Monographs and Reviews

3201 Fried BM: Primary carcinoma of the lung. Bronchiogenic cancer - a clinical and pathological study in two parts. Baltimore: Williams & Wilkins Co., 247 pages, 1932. [Cited P163]

1932 Periodicals

3211 Nolan LE: A statistical study of 1,250 autopsies in Veterans' Administration Hospitals. Med Bull Vet Adm 9: 124-141, 1932. [Cited P181]

3212 Rogers WL: Primary cancer of the lung. A clinical and pathologic survey of fifty cases. Arch Intern Med 49: 1058-1077, 1932. [Cited P181]

3213 Freeman W: Primary carcinoma of the lung with cerebral metastases. Report of four cases. Med Ann D.C. 1: 58-62, 1932.

3214 Young DA, Lord FT, Mallory TB: An unusual association of two lung disease processes - Case 18482. N Engl J Med 207: 993-994, 1932.

3215 Vinson PP: Primary carcinoma of the bronchus: report of seventy-one cases in which the diagnosis was made by bronchoscopic examinations. Minn Med 15: 15-17, 1932. [Cited P181]

3216 Moses HM: Primary carcinoma of the lung. Int Clin 3: 34-45, 1932. [DMA 543]

3217 Wessler H, Rabin CB: Benign tumors of the bronchus. Am J Med Sci 183: 164-180, 1932. [Cited P90]

3218 Williams HB: Nontuberculous lung diseases; a report of three cases: coccidiosis, actinomycosis, carcinoma. Med Bull Vet Adm 8: 435-441, 1932.

3219 Manges WF: Primary carcinoma of the lung. Roentgen diagnosis and preliminary report of roentgen therapy. Am J Roentgenol 27: 858-869, 1932.

3220 Duhig JV: Primary cancer of the lung. A review, with a study of two cases. J Cancer Res Comm Univ Sydney 4: 53-64, 1932.

2062855424

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3221 Kerley P: Malignant disease of the lungs: radiographic features. Br Med J 1: 416-419, 1932. [Cited P181]

3222 Brockbank W: The occupational incidence of primary lung cancer. Q J Med (Oxford) 1: 31-40, 1932. [Cited P181, P244; DMA 523a]

3223 Tyler AF: The treatment of bronchial carcinoma by electrocoagulation, radium implants and high voltage x-ray. Arch Phys Ther 13: 69-74, 1932. [Cited P181]

3224* McNally WD: The tar in cigarette smoke and its possible effects. Am J Cancer 16: 1502-1514, 1932. [SOA 159; ERR P398; Cited P81, P90, P181, P214, P244, P289, P291; WHM]

3225 Boycott AE: Cancer of the lung. Lancet 959, October 29, 1932.

3226 Editorial: The increase in cancer of the lung. Lancet 222: 1206-1207, 1932. [Cited P244]

3227 Bogen E, Loomis RN: Tobacco tar: an experimental investigation of its alleged carcinogenic action. Am J Cancer 16: 1515-1521, 1932. [SOA 28; ERR P28; TOP P1551; DTH Exhibit 48 page 399; WHM 399]

3228 Roffo AH: Carcinome developpe chez un lapin apres trois ans, par l'effet du tobac. Neoplasmes 11: 77-89, 1932. [SOA 226; P226; TOP 2048; Cited P81]

3229 Roffo AH: Carcinoma desarrollado en un conejo fumador a lost res anos. Bol Inst Med Exp 7: 545-573, 1932. [SOA 225; TDH Exhibit 58, 59; Cited P81, P175, P229, P235]

3230* Cooper EA, Lamb FWM, Sanders E, Hirst EL: The role of tobacco smoking in the production of cancer. J Hyg 32: 293-300, 1932. [SOA 45; P45; ERR 29; DTH Exhibit 70; TOP 1562; Cited P81, P159, P175, P244, P245, P264, P291, P398; WHM 130]

3231 Hueper WC, Russell M: Some immunologic aspects of leukemia. Arch Intern Med 49: 113-122, 1932.

3232 Kirklin BR: Roentgenologic signs and differential diagnosis of the principal malignant diseases of the lungs and mediastinum. Wisconsin Med J 31: 95-99, 1932.

3233* Cook JW, Hieger I, Kennaway EL, Mayneord WV: The production of cancer by pure hydrocarbons - Part I. Proc R Soc Edinburgh Sect B 111: 455-484, 1932. [Ref. in Harris' 1987 article; Cited P245, P264]

3234 Pancoast HK, Pendergrass EP: Primary bronchogenic carcinoma of the lungs. Report of a new technique in radiation therapy with comments on endoscopic radon implantation. Am J Roentgenol 27: 357-361, 1932.

2062855425

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3235 Butler PF, Ritvo M: Primary carcinoma of the lung. Diagnosis and treatment with the x-ray. New Eng J Med 207: 435-443, 1932. [DMA 526; Cited P181]

3236 Pirchan A, Sikl H: Cancer of the lung in the miners of Jachymov (Joachimstal). Report of cases observed in 1929-1930. Am J Cancer 16: 681-722, 1932. [Cited P181, P290]

3237 Klotz O, Simpson W: Silicosis and carcinoma of the lung. Lib Manniv 2: 685-692, 1932.

3238 Gloyne SR: The pathology of malignant disease of the lung and pleura. Postgrad Med J Lond 8: 103-109, 1932.

3239 Gardner LU: Studies on experimental pneumonokoniosis. Viii. Inhalation of quartz dust. J Ind Hyg 14: 18-38, 1932.

3240 Fried BM: Chronic pulmonary osteoarthropathy. Dyspituitarism as a probable cause. Arch Intern Med 72: 565-580, 1932. [DMA 584]

3241 Campbell JA: The effect of carbon monoxide and other agents upon the rate of tumour growth. J Pathol Bacteriol 35: 379-394, 1932. [Cited P38]

3242 Pancoast HK: Superior pulmonary sulcus tumor. Tumor characterized by pain, Horner's syndrome, destruction of bone and atrophy of hand muscles. JAMA 99: 1391-1396, 1932.

1933 Mongraphs and Reviews

3301 Bigelow GH, Lombard HL: Cancer and other chronic diseases in Massachusetts. Boston: Houghton Mifflin Co. 355 pages, 1933. [SOA 23; TDH Exhibit 38 page 278; Cited P208]

3302 Hruby AJ, Sweany HC: Primary carcinoma of the lung - with special reference to incidence, early diagnosis and treatment. Arch Intern Med 52: 497-540, 1932. [DMA 541; Cited P181]

1933 Periodicals

3311 Hueper WC, Allen A, Russell M, Woodward G, Platt M: Studies of growth factors of embryo extract. Am J Cancer 17: 74-105, 1933.

3312 Harding DB: Primary carcinoma of the lung. Kentucky Med J 31: 524-525, 1933.

3313 Hamman L: The diagnosis of carcinoma of the lung. Am Rev Tuberc 28: 711-733, 1933. [Cited P181]

2062855426

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3314 Overholt RH: Primary carcinoma of the lung. Surgical extirpation. Am J Surg 22: 181-186, 1933.

3315 Churchill ED: The surgical treatment of carcinoma of the lung. J Thorac Surg 2: 254-266, 1933.

3316 Simons EJ: Primary carcinoma of the lungs. Minn Med 16: 1-6, 1933.

3317 Leddy ET, Vinson PP: The roentgen treatment of bronchiogenic carcinoma. Am J Roentgenol 30: 92-94, 1933. [Cited P181]

3318 Carlson HA, Ballon HC: The operability of carcinoma of the lung. J Thorac Surg 2: 323-248, 1933.

3319 Graham EA, Singer JJ: Successful removal of an entire lung for carcinoma of the bronchus. JAMA 101: 1371-1374, 1933. [Cited P180, P181, P334, P379]

3320 Neuhof H: The operative treatment of cancer of the lung. Surg Clin NA 13: 365-378, 1933.

3321 Lilienthal H: Pneumonectomy for sarcoma of the lung in a tuberculous patient. J Thorac Surg 2: 600-611, 1933. [Cited P180, P181]

3322 Lloyd MS: Bronchial carcinoma. J Thorac Surg 3: 208-209, 1933.

3323 Kernan JD, Cracovaner AJ: Carcinoma in a lung abscess cavity. Laryngoscope 43: 501-503, 1933.

3324 Bradshaw HH: Carcinoma of the lungs. Clin Rev Pittsburgh 2: 49-55, 1933.

3325 Clerf LH, Crawford BL: Bronchogenic carcinoma - with special reference to classification, prognosis and treatment. J Thorac Surg 3: 73-85, 1933.

3326 Beardsley JM: Primary carcinoma of the lung in a child. Can Med Assoc J 29: 257-259, 1933.

3327 Pilcher JF, Brindley P: Primary carcinoma of the lungs. Report of ten cases. Texas State J Med 29: 247-253, 1933.

3328 Gutteridge E: Primary carcinoma of the lung: a report of thirty-six cases from the Melbourne Hospital records, 1922-1932. Melbourne Hosp Clin Rep 4: 16-22, 1933.

2062855427

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3329 Roberts F: X-ray treatment of malignant disease of the lung. Br Med J 2: 142-146, 1933. [Cited P181]

3330* Stocks P, Karn MN: A co-operative study of the habits, home life, dietary and family histories of 450 cancer patients and of an equal number of control patients. Ann Eugenics 5: 237-280, 1933.

3331+ Ferrari E: Tabakrauch und Lungenkarzinom. Munch Med Wochenschr 80: 942-932, 1933. [Cited P181]

3332* Hueper WC, Itami S: Effects of neoarsphenamine on spontaneous breast tumors of mice. Am J Cancer 17: 106-115, 1933.

3333* Cook JW, Hewitt CL, Hieger I: The isolation of cancer-producing hydrocarbon from coal tar. J Chem Soc 1: 395-405, 1933.

3334 Watson AF: Experimental skin tumours in the rat produced by tar. J Pathol Bacteriol 36: 251-256, 1933. [SOA 282; Cited P81]

3335 Shope RE, Hurst EW: Infectious papillomatosis of rabbits - with a note on the histopathology. J Exp Med 58: 607-624, 1933.

3336 Sladden AF: The silica content of lungs. Lancet 2: 123-125, 1933. [Cited P181]

3337 Banks HS, Weir JH: Chronic pulmonary catarrh and fibrosis in school children. Tubercle 14:385-390, 1933.

1934 Monographs and Reviews

3401 Emerson CP: New growths in the lungs. In: A Text-book of Medicine by American Authors, RL Cecil, editor. Phildadelphia: WB Sauders Co, 905-906, 1934.

3402+ Sannie C, Truhaut R: Les agents chimiques cancerigenes. Bull Assoc Canc 23: 6-37, 1934.

1934 Periodicals

3411 Floridis GG, Nixon CE, Ginsburg HM: Primary carcinoma of the lung with unusual manifestation. Calif West Med 40: 365-367, 1934.

3412 Bronfin ID: Primary carcinoma of the lung simulating pulmonary tuberculosis. Colo Med 31: 193-200, 1934.

3413 King CV: Primary carcinoma of the lung. A review with report of illustrative cases. Med Ann DC 3: 36-41, 1934.

3414 Steiner PE, Francis BF: Primary apical lung carcinoma. Am J Cancer 22: 776-785, 1934.

2062855428

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3415 Gould LK: Primary cancer of the lung - with report of a case in a boy aged ten. J Ind Med Assoc 27: 332-334, 1934. [Cited P181]

3416 Jermain WM: Primary carcinoma of the lung. Wis Med J 33: 205-209, 1934.

3417 Geschickter CF, Denison R: Primary carcinoma of the lung. Am J Cancer 22: 854-877, 1934. [Cited P181]

3418 Rienhoff WF Jr, Broyles EN: The surgical treatment of carcinoma of the bronchi and lungs. JAMA 103: 1121-1129, 1934.

3419 Overholt RH: The total removal of the right lung for carcinoma - report of a successful case. J Thorac Surg 4: 196-210, 1934. [Cited P180, P181]

3420 Churchill ED: Primary carcinoma of the lung. Common Health Boston 21: 279-282, 1934.

3421 Means JH: Carcinoma of the lung. N Engl J Med 211: 890-893, 1934.

3422 Chapman EM, Mallory TB: Cabot Case 20512 - Carcinoma of the lung. N Engl J Med 211: 1164-1166, 1934.

3423 Allen CI: A case of primary carcinoma of the lung. Report four years after lobectomy. J Thorac Surg 4: 224-230, 1934.

3424 Tuttle WMc, Womack NA: Bronchogenic carcinoma: a classification in relation to treatment and prognosis. J Thorac Surg 4: 125-146, 1934. [Cited P181]

3425 Hirsch EF: Cryptic bronchogenic carcinoma of the lung. Med Clin NA 17: 1527-1532, 1934.

3426 Eggers C: Lobectomy for carcinoma of the lung. J Thorac Surg 4: 211-217, 1934.

3427 Crowell LA: Primary carcinoma of the lung in a twenty-three year old man. JAMA 102: 927-928, 1934.

3428 Rabin CB, Neuhof H: A topographic classification of primary cancer of the lung. Its application to the operative indication and treatment. J Thorac Surg 4: 147-164, 1934. [Cited P181, P163]

3429 Klinck GH Jr, Jacobsen VC: Primary carcinoma of the lung. Arch Pathol 17: 717-718, 1934.

3430 Maxwell I: Silicosis and carcinoma of the lung. Med J Australia 2: 168-169, 1934. [Cited P181]

2062855429

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3431 Meakins JC: The early diagnosis of carcinoma of the lung. Can Med Assoc J 3: 283-285, 1934.

3432 Edwards AT: Malignant disease of the lung. West London Med J 39: 213-230, 1934.

3433 Edwards AT: Malignant disease of the lung. J Thorac Surg 4: 107-124, 1934. [Cited P180]

3434 Edwards T: Selected cases of intrathoracic tumours. 1. A case of primary carcinoma much improved by thoracotomy and radon. Brompton Hosp Rep Lond 3: 154-155, 1934.

3435 Edwards AT: Cancer of the lungs and pleurae. Practitioner 143: 29-39, 1934.

3436 Dible JH: Silicosis and malignant disease. Lancet 2: 982-983, 1934. [Cited P131, P132, P181]

3437 Hill RM: Primary cancer of the lung: its incidence and pathology. Edinburgh Med J 51: 320-333, 1934.

3438 Sears WG: Carcinoma of the lung. Clinic J London 63: 328-334, 1934.

3439 Young A: Primary carcinoma of the lung. Report of a case of primary carcinoma of the upper lobe of the left lung, treated successfully by lobectomy, and subsequent thoracoplasty. Ann Surg 100: 1-10, 1934.

3440 Scadding JG: Carcinoma of lung: Morecellement removal by bronchoscopy; subsequent radon treatment. Proc R Soc Med 28: 1183-1184, 1934.

3441 Fried BM: Bronchiogenic cancer: treatment with roentgen rays. Am J Cancer 20: 791-806, 1934.

3442 Strode JE: Successful removal of an entire lung for carcinoma. J Mo Med Assoc 31: 34, 1934.

3443 Jackson CL, Konzelmann FW: Bronchial carcinoma. Bronchoscopic biopsy in a series of 32 cases. J Thorac Surg 4: 165-195, 1934. [Cited P180, P181, P278, P334]

3444 Sweany HC: Primary bronchiogenic carcinoma: incidence, pathogenesis and diagnosis. Ann Otol Rhinol Laryngol 43: 561-571, 1934.

3445 Sweany HC: So-called alveolar cell carcinoma of the lung. Trans Chicago Pathol Soc 14: 165-166, 1934.

3446 Ellis R: Carcinoma of the lung. Clin J London 63: 110-115, 1934.

2062855430

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3447+ Lu-Fu-hua: Uber die Erzeugung von Krebs durch Tabakteerpinselung beim Kaninchen. II. Uber das Solitarauftretern einzelner Tumoren auf einer diffus gereizten Korperstelle. Frankfurt Z Pathol 47: 52-62, 1934. [ERR 22, P399; Cited P81, P181, P175, P264, P291; WHM 263]

3448 Hueper WC: Leukemoid and leukemic conditions in white mice with spontaneous mammary carcinoma. Folia Haematol 52: 167-178, 1934.

3449 Hueper WC: Significance of sulphydryl as a growth factor. Arch Pathol 17: 218-242, 1934.

3450 Hueper WC: Cancer of the urinary bladder in workers of chemical dye factories and dyeing establishments: a review. J Ind Hyg 16: 255-281, 1934.

3451 Sugiura K: Reaction of transplantable mouse sarcoma No. 180 to radiations of different wave lengths (200 KV. roentgen rays and gamma rays). Am J Roentgenol 31: 614-627, 1934. [Cited P264]

3452 Allen ML: Bronchiogenic carcinoma associated with pneumoconiosis: a report of two cases. J Ind Hyg 16: 346-347, 1934. [Cited P181]

3453 Campbell JA: Cancer of skin and increase in incidence of primary tumours of lung in mice exposed to dust obtained from tarred roads. Br J Exp Pathol 15: 287-294, 1934. [Cited P38, P39, P131, P132, P158, P290]

3454 Twort CC: On the prevention of mineral oil and tar dermatitis and cancer. Lancet 1: 286-287, 1934.

3455 Bourne MC, Young L: CXII. The metabolism of naphthalene in rabbits. Biochem J 28: 803-808, 1934.

3456 Weir P, Little CC: The incidence of uterine cancer in Jews and Gentiles. Bull Am Soc Control Cancer 16: 6-7, 1934. [ERR 24]

3457 Riddell AR: The clinical aspects of simple silicosis and silicosis with tuberculosis. Am Rev Tuberc 29: 36-42, 1934.

3458 Bonser GM: The incidence of intrathoracic tumours in Leeds. J Hyg 36: 218-234, 1934.

1935 Monographs and Reviews

3501 Greenwood J: Epidemics and Crowd-Diseases. New York: MacMillan Co. 379 pages, 1935.

3502 Graham EA, Singer JJ, Ballon HC: Surgical Diseases of the Chest. Chapter 17. Tumors of the lung. Philadelphia: Lea & Febiger, 806-852, 1935. [Cited P181]

2062855431

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

1935 Periodicals

3511 Ewing J: The modern attitude toward traumatic cancer. Bull NY Acad Med 11: 281-334, 1935.

3512 Matthews WM: Carcinoma of lower lobe of left lung, involving the peribronchial and hilus glands and perforating the left cardiac auricle. Med Bull Vet Adm 12: 81-83, 1935.

3513 Sweany HC: A so-called alveolar cell cancer of the lung. Arch Pathol 19: 203-207, 1935. [Cited P338]

3514 Leader SA: The coexistence of primary carcinoma of the lung and pulmonary tuberculosis with a case report. Med Bull Vet Adm 12: 78-80, 1935.

3515 Louis DJ: Primary bronchogenic carcinoma with metastases: Report of a case. Ill Med J 67: 552-554, 1935.

3516 Jaffe RH: The primary carcinoma of the lung. A review of 100 autopsies. J Lab Clin Med 20: 1227-1237, 1935. [Cited P163, P180, P181, P278; DMA 540]

3517 Wood LE, Spake LB, Summerville WW, Tice GM: Primary bronchogenic carcinoma. J Kan Med Soc 36: 227-234, 1935. [Cited P181]

3518 Gorman CE: Primary carcinoma of the lung - case reports. New Orleans Med Surg J 88: 471-473, 1935.

3519 Warner CG: Primary carcinoma of the lung. Report of 11 cases with a study of the pathology. Bull Sch Med Univ Maryland 19: 89-101, 1935.

3520 Overholt RH: Pneumonectomy for malignant and suppurative disease of the lung. With a report of eight cases. J Thorac Surg 5: 54-75, 1935. [Cited P180, P181]

3521 Churchill ED, Holmes GW, King DS: Cabot Case 21291: Carcinoma, epidermiod, bronchiogenic, left upper lobe. N Engl J Med 213: 122-125, 1935. [DMA 528]

3522 Olson KB: Primary carcinoma of the lung. A pathological study. Am J Pathol 11: 449-468, 1935. [Cited P181, P334]

3523 Samson PC: Entdifferentiation in bronchogenic carcinoma. Am J Cancer 23: 741-753, 1935. [Cited 181]

3524 Alexander J: Observations on total pulmonary lobectomy and pneumonectomy. Ann Surg 101: 393-406, 1935. [Cited P180]

3525 Simons EJ: Primary carcinoma of the lung: etiological concepts. Lancet 55: 637-640, 1935.

2062855432

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3526 Neely JM: Primary carcinoma of the lung. A pathological and clinical study based on eighty cases. Neb Med J 20: 247-252, 1935.

3527 Orton HB: Primary carcinoma of the lung - peroral endoscopic study. J Med Soc NJ 32: 635-638, 1935. [DMA 524]

3528 Klein W: Symposium on primary carcinoma of the lung. Roentgen diagnosis of primary carcinoma of the lung. J Med Soc NJ 32: 631-634, 1935.

3529 Fine MJ, Jaso JV: Silicosis and primary carcinoma of the bronchus. Report of case. JAMA 104: 40-43, 1935.

3530 Andrus WD: Report of the chest tumor registry. J Thorac Surg 4: 236-250, 1935.

2531 Frissell LF: Primary carcinoma of the lung. NY State J Med 35: 851-859, 1935.

3532 Smith WA: The clnical aspect of primary pulmonary carcinoma. J South Carolina Med Assoc 31: 169-173, 1935.

3533 Heacock CH, King JC: The diagnosis of primary carcinoma of the lung. Radiology 24: 452-462, 1935. [Cited P181]

3534 Dudgeon LS, Wrigley CH: On the demonstration of articles of malignant growth in the sputum by means of the wet-film method. J Laryngol Otol 50: 752-763, 1935. [Cited P180, P181, P379]

3535 Matheson NM: Primary carcinoma of bronchus. Massive involvement of heart and pericardium. Br J Radiol 8: 248-251, 1935.

3536+ Becchini G: Studio in terma di cancerologia polmonare primitive. Policlinico 42: 89-111, 1935.

3537 Passey RD, Holmes JM: The incidence of intrathoracic neoplasia in the teaching hospitals of Great Britain 1894-1928. Q J Med 4: 321-344, 1935. [Cited P58, P131, P181, P278]

3538 Moore RA: The morphology of small prostatic carcinoma. J Urol 33: 224-234, 1935. [Cited P131]

3539 Sweany HC: The pathogenesis of primary cancer of the lung. Am J Clin Pathol 5: 1-12, 1935.

3540+ Thys F: Note sur l'etiologie du carcinome bronchique. Rev Belge Sci Med 7: 640-644, 1935. [SOA 266; P266]

3541 Anon: The Fortune Survey. III. Cigarettes. Fortune Magazine 12(1): 68, 111-116, 1935. [Cited in Harris' 1987 article]

2062855433

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3542 Schurch O, Winterstein A: Experimentelle Untersuchungen zur Frage Tabak und Krebs. Z Krebforsch 42: 76-92, 1935. [SOA 245; P245; TDH Exhibit 45, 46 page 362; TOP 1549-1551; Cited P39, P61, P81, P264]

3543 Saccone A, Hendler HB: Primary carcinoma of the lung. Coll Papers NY Homeop Med Coll 1: 513-524, 1935.

3544* Barry G, Cook JW, Haslewood GAD, Hewett CL, Hieger I, Kennaway EL: The production of cancer by pure hydrocarbons - Part III. Proc R Soc 117: 315-351, 1935. [SGR 18]

3545 Twort CC, Twort JM: Induction of cancer by cracked mineral oils. Lancet 2: 1226-1228, 1935.

3546 Mottram JC: On the origin of tar tumours in mice, whether from single cells or many cells. J Pathol Bacteriol 40: 407-414, 1935.

3547 Fried BM: Bronchiogenic cancer combined with tuberculosis of the lungs. Am J Cancer 23: 247-266, 1935. [Cited P181]

3548 Andervont HB: Further studies on the production of dibenzanthracene tumors in pure strain and stock mice. Pub Health Rep 50: 1211-1217, 1935. [Cited P38, P131, P264]

3549 Bittner JJ: The breeding behavior and tumor incidence of an inbred albino strain of mice. Am J Cancer 15: 113-121, 1935. [Cited P38]

3550* Montgomery H: Arsenic as an etiologic agent in certain types of epithelioma. Arch Dermatol Syphilol 32: 218-236, 1935.

3551 Fried BM: Primary carcinoma of the lungs. Am J Surg 29: 261-262, 1935.

3552 Teleky L: Injurious factors in asbestosis and silicosis. J Ind Hyg 17: 32-33, 1935.

3553 Dieffenbach RH: The surgical treatment of primary carcinoma of the lung. J Med Soc NJ 32: 645-648, 1935.

3554 Stekol JA: Metabolism of naphthalene in adult and growing dogs. J Biol Chem 110: 463-469, 1935.

3555 Lynch KM, Smith WA: Pulmonary asbestosis III. Carcinoma of lung in asbestos-silicosis. Am J Cancer 24: 56-64, 1935. [ERR 50; Cited P131, P132, P163, P181, P290, P334]

3556 Gloyne SR: Two cases of squamous carcinoma of the lung occurring in asbestosis. Tubercle 17: 5-10, 1935. [Cited P131, P132]

3557+ Morpurgo B: Künstliche Erzeugung eines sehr atypischen Myoblastoms der Zunge bei einer weissen Ratte. Z Path Anat 63: 1-5, 1935. [Cited P18]

2062855434

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

1936 Monographs and Reviews

3601+ Seele H: Das primare Lungencarcinom. Berlin: Neuland Druck, 1-31, 1936.

3602 Edwards AT: Chapter 5. Diagnosis of malignant disease of the lung and mediastinum. In: The early diagnosis of malignant disease - for the use of general practitioners, Donaldson M, Cade S, Harmer WD, Ward RO,Edwards AT. London: Humphrey Milford, 711-80, 1936.

3603 Craver LF: Carcinoma of the lung. In: Diseases of the respiratory tract. Eighth annual graduate fortnight of the New York Academy of Medicine. Philadelphia: WB Sauders Co., 349-364, 1936. [Cited P334]

1936 Periodicals

3611 Shuman W: Lung cancer. Med Rec 144: 83-84, 1936.

3612 Fennel EA: Primary lung cancer. Proc Clin Honolulu 2: 1-11, 1936.

3613 Arkin A, Wagner DH: Primary carcinoma of the lung. A diagnostic study of one hundred and thirty-five cases in four years. JAMA 106: 587-591, 1936. [SOA 6; P6; TOP 822; Cited P90, P181, P214, P244,P278, P289, P344]

3614 Overholt RH: Primary carcinoma of the lung: Early diagnosis and treatment by pneumonectomy. N Engl J Med 214: 93-100, 1936.

3615 Churchill ED: Lobectomy and pneumonectomy in bronchiectasis and cystic disease. J Thorac Surg 6: 286-311, 1936. [Cited P181]

3616 Glenn EE: Primary carcinoma of the lung. Dis Chest 2: 14-16; 38, 1936.

3617 Graham EA: Primary carcinoma of the lung or bronchus. Ann Surg 103: 1-12, 1936. [Cited P180, P181]

3618 Graef I, Steinberg I: Superior pulmonary sulcus tumor. A case exhibiting a malignant epithelial neoplasm of unknown origin with Pancoast's syndrome. Am J Roentgenol 36: 293-300, 1936. [Cited P334]

3619 Lyle HM: Carcinoma of the right lung. Pneumectomy in one stage. Ann Surg 103: 124-129, 1936. [Cited P180, P181]

3620 Kramer R, Som ML: Bronchoscopic study of carcinoma of the lung. An analysis of three hundred cases of bronchial carcinoma with one hundred postmortem examinations. Arch Otolaryngol 23: 526-543, 1936. [Cited P163, P181, P278]

3621 Rosedale RS, McKay DR: A study of 57 cases of bronchogenic carcinoma. Am J Cancer 26: 493-506, 1936. [Cited P163]

2062855435

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3622 Frost TT, Wolpaw SE: Intrathoracic sympathoblastoma. Producing the symptomatology of a superior pulmonary sulcus tumor (Pancoast). Am J Cancer 26: 483-492, 1936. [Cited P334]

3623 Marcil GE, Crawford BL: Primary carcinoma of the lung occurring in the apex. Report of one case. Am J Cancer 26: 137-142, 1936.

3624 Flick JB, Gibbon JH Jr: Total removal of the left lung for carcinoma. Ann Surg 103: 130-134, 1936. [Cited P180, P181]

3625 Nelson K: Pulmonary tuberculosis and primary carcinoma of the lung; report of two cases. Virginia Med Month 63: 530-536, 1936.

3626 Rice CM: Primary carcinoma of the lung. Review of thirty cases. J Lab Clin Med 21: 906-909, 1936. [Cited P163, P181]

3627 Fleckseder R: Ueber den Bronchialkrebs und einige seiner Entstehungsbedingungen. Munch Med Wochenschr 83: 1585-1588, 1936. [SOA 78; P78]

3628 Wood D: Carcinoma of the bronchus. The treatment of carcinoma of the lung. Bristol Med Chir J 53: 145-150, 1936.

3629 Holmes AH: Pulmonary carcinoma from the clinical standpoint. Med Press Circ Dublin 192: 281-285, 1936.

3630 El Gazayerli M: Observations of primary lung carcinoma. Edinburgh Med J 43: 636-640, 1936. [Cited P181]

3631 Ehrlich DE, Hauptman HA: Primary carcinoma of the lung. Radiology 26: 563-573, 1936.

3632 Kennaway NM, Kennaway EL: A study of the incidence of cancer of the lung and larynx. J Hyg London 36: 236-267, 1936. [SOA Key 131; TDH Exhibit 82 page 607; TOP 1566; Cited P39, P90, P131, P132, P181, P278, P289]

3633 Reinhoff WF Jr: The surgical technic of total pneumonectomy. Arch Surg 32: 218-231, 1936. [Cited P180]

3634 Reinhoff WF Jr: The treatment of carcinoma of the lung. Surg Clin NA 16: 1459-1479, 1936. [Cited P180]

3635 Bush GB: Primary carcinoma of the lung radiologically considered. Bristol Med Chir J 53: 131-136, 1936.

3636 Campbell JA: The influences of breathing carbon monoxide and oxygen at high percentages for prolonged periods upon development of tar cancer in mice. J Pathol Bacteriol 36: 243-248, 1936.

2062855436

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3637 Beard HH, Boggess TS, Haam EV: Experimental production of malignant tumors in the albino rat by means of ultraviolet rays. Am J Cancer 27: 257-266, 1936. [Cited P264]

3638 Egbert DS, Geiger AJ: Pulmonary asbestosis and carcinoma. Report of a case with necropsy findings. Am Rev Tuberc Pulm Dis 34: 143-150, 1936. [Cited P132, P181]

3639 Hueper WC: Allergy and neoplasia with special reference to occupational tumor formation. J Ind Hyg Toxicol 18: 140-157, 1936.

3640* Wiley FH, Hueper WC, von Oettingen WF: The toxicity and potential dangers of ethylene glycol. J Ind Hyg Toxicol 18: 123-126, 1936.

3641 Gloyne SR: A case of oat cell carcinoma of the lung occurring in asbestosis. Tubercle 18: 100-101, 1936. [Cited P181]

3642 Campbell JA: The effects of exhaust gases from internal combustion engines and of tobacco smoke upon mice, with special reference to incidence of tumours of the lung. Br J Exp Pathol 17: 146-158, 1936. [SOA 38, Key P38, DTH Exhibit 72 page 526; TOP 1563; DMA 423; Cited P39, P53, P81, P181, P244, P264, P291]

3643 Anon: Exhaust gas and smoke. Lancet 2: 31, 1936.

3644 Passey RD, Leese A, Knox JC: Bronchiectasis and metaplasia in the lung of the laboratory rat. J Pathol Bacteriol 42: 425-434, 1936. [Cited 181]

3645 Schrire T: Primary carcinoma of the lung. S Afr Med J 10: 475-478, 1936.

3646 Roffo AH: El tobaco como carcerigeno. Bol Inst Med Exp 13: 287-333, 1936. [SOA 227; TOP 2048; Cited P81, P229, P234, P235, P264, P291; French version is 3731; German version is 3733]

3647 Rous P, Kidd JG: The carcinogenic effect of a virus upon tarred skin. Science 83: 468-469, 1936. [Cited in Harris' 1987 article]

3648 Seelig MG, Benignus EL: Coal smoke soot and tumors of the lung in mice. Am J Cancer 28: 96-111, 1936. [Cited P181, WHM 191]

3649 Furth J, Furth OB: Neoplastic diseases produced in mice by general irradiation with x-rays. I. Incidence and types of neoplasms. Am J Cancer 28: 54-65, 1936. [SGR 124]

3650 Heine LH: The effect of radiation upon ciliated epithelium. Ann Otol Rhinol Laryngol 45: 60-74, 1936. [WHM 469]

3651 Little CC: The constitutional factor in cancer. Bull Am Soc Control Cancer 18: 11-12, 1936. [ERR 24]

2062855437

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3652 Little CC: Diet and cancer. Bull Am Soc Control Cancer 18: 9-10, 1936. [ERR 24]

3653* Bogen E: Irritant factors in tobacco smoke. Calif West Med 45: 342-346, 1936. [SOA 26; key P26; TOP 866]

1937 Monographs and Reviews

3701 Hoffman FL: Cancer and diet - with facts and observations on related subjects. Baltimore: Williams & Wilkins Co., 1-765, 1937. [ERR 35; Cited P152]

3702 Simons EJ: Primary carcinoma of the lung. Chicago: Year Book Publishers, Inc. 1-263, 1937. [P58, P81, P158, P163, P181]

3703 Soliman A: Contribution a l'etude du cancer primitif du poumo. Lausanne: Imprimerie A Bovard-Giddey, 1-29, 1930.

3704 Jackson C, Jackson CL: The larynx and its diseases. Philadelphia: WB Saunders Co., 49-63, 370-388, 1937. [1939 edition cited in P385; Cited P181, P244]

3705 Frissell LF, Knox LC: Primary carcinoma of the lung. Am J Cancer 30: 219-288, 1937. [Cited P180, P181, P214]

1937 Periodicals

3711 Kinoshita R: Special report: Studies on the cancerogenic chemical substances. Trans Jpn Pathol Soc 27: 665-725, 1937. [SOA 128, Key P400a; Cited P81, P264, P291; WHM 259 (secondary ctation slips not completed)]

3712 Jack CM: Some unusual features of lung cancer. Ill Med J 71: 315-318, 1937.

3713 Scheele MH: Cancer of the lung. J Iowa Med Soc 27: 636-638, 1937.

3714 Overholt RH: Clinical investigation of primary malignancy of the lung: diagnosis and operability. Surg Clin NA 17: 895-904, 1937. [DMA 529]

3715 Pierce CB, Ingersoll CF: Bronchogenic carcinoma. Ind Med 6: 411-422, 1937. [Cited P181]

3716 Leucutia T: Treatment of carcinoma of the lung. J Michigan Med Soc 36: 470-472, 1937.

3717 Brines OA: Primary carcinoma of the lung - pathology. J Michigan Med Soc 36: 468-469, 1937.

3718 Craver LF: Primary carcinoma of the lung. J Med Soc NJ 34: 598, 1937.

2062855438

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3719 Mattick WL, Burke EM: Primary carcinoma of the lung. A pathologic and radiologic study. Rev Tum Ther 1: 49-57, 1937; JAMA 109: 2121-2124, 1937. -[Cited P163,P181]

3720 Bliss TL: Bronchorrhea. Its occurrence in a case of bronchogenic carcinoma. J Thorac Surg 6: 660-665, 1937.

3721 Clerf LH: Carcinoma of the bronchus. Radiology 28: 438-444, 1937. [Cited P181]

3722 Charr R: Carcinoma of the bronchus in association with anthraco-silicosis. A study of four cases. Am J Med Sc 194: 535-541, 1937. [Cited P163, P181, P334]

3723 Farrell JT Jr: Primary bronchial carcinoma and pulmonary metastasis compared clinically and roentgenologically. Radiology 28: 445-449, 1937. [Cited P181]

3724 Husted E, Biilmann G: Primary cancer of the lung - with reference to the frequency, etiology, pathological anatomy and histology of this lesion. Acta Pathol 14: 141-196, 1937.

3725 Ameuille & Fauvet: Noncancerous consolidations in pulmonary cancer. JAMA 109: 443-445, 1937.

3726 Tchaperoff ICC: The diagnosis and treatment of primary cancer of the lung. St Thomas Hosp Rep London 2: 233-248, 1937.

3727 Ormerod FC: The pathology and treatment of carcinoma of the bronchus. J Laryngol Otol 52: 733-745, 1937. [Cited P181]

3728 Craig JW: Hypertrophic pulmonary osteoarthropathy as the first syymptom of pulmonary neoplasm. Br Med J 1: 750-752, 1937.

3729 Donald WM: Cancer of the lung: historical and medical aspects. J Michigan Med Soc 36: 472-474, 1937.

3730 Editorial: Cancer of the lung. JAMA 108: 1716-1717, 1937.

3731 Roffo AH: Le tabac, agent cancerigene. Acta Unio Int Cancr Louvain 2: 45-60, 1937. [SOA 231; P231; DTH Exhibit 56, 57 page 451; TOP 2048; German version is 3733; Spanish version is 3646]

3732 Roffo AH: Expectrografia de los derivados obtenidos por destilacion directa de los tabacos y su relacion como agentes cancerigenos. Bol Inst Med Exp 14: 311-399, 1937. [SOA 229; TOP 2048; Cited P81, P235, P264]

3733 Roffo AH: Der Tabak als krebserzeugendes Agens. Dtsch Med Wochenschr 63: 1267-1271, 1937. [SOA 228, Key P231; DTH Exhibit 60, 61; Cited P39, P81, P90, P175, P235, P289; French version is 2731; Spanish version is 3646]

2062855439

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3734 Schurch O, Winterstein A: Experimenteller Beitrag zur Grage Tabak und Krebs. Z Krebsforsch 46: 414-419. 1937. [SOA 246, Key P246; TOP 2048; Cited P81, P264, P291]

3735 Evans EE: Causative agents and protective measures in the anilin tumor of the bladder. J Urol 38: 212-215, 249-250, 1937.

3736 Kenning JC: Primary carcinoma of the lung. J Michigan Med Soc 36: 466-468, 1937.

3737 Taki S: Carcinogenicity of substance isolated from tobacco tar. Report on regular meeting held 2/20/1937 (translated from Japanese). Osaka Dai Iga Zas 36: 483-484, 1937.

3738 Kuroda S: Occupational pulmonary cancer - of generator gas workers. Ind Med 6: 304-306, 1937.

3739* Hieger I: The fluorescence spectrum of 3:4-benzpyrene. Am J Cancer 29: 705-714, 1937.

3740* Bachman WE, Cook JW, Dansi A, Worms CGM, Haslewood GAD, Hewett CL, Robinson AM: The production of cancer by pure hydrocarbons - IV. Proc Royal Soc London 123: 343-368, 1937.

3741* Cook JW, Haslewood GAD, Hewett CL, Hieger I, Kennaway EL, Mayneord WV: Chemical compounds as carcinogenic agents. Am J Cancer 29: 219-259, 1937. [Cited P81; ERR 27]

3742 Campbell JA: Cancer of the human lung and animal experiment. J Ind Hyg 19: 449-462, 1937.

3743 Campbell JA: The effects of road dusts "freed" from tar products upon the incidence of primary lung-tumours of mice. J Ind Hyg 18: 215-223, 1937. [Cited P39]

3744 Boyland E, Warren FL: The induction of tumours by methyl-cholanthrene in two strains of mice. J Pathol Bacteriol 45: 171-177, 1937. [Cited P264]

3745 Andervont HB: Pulmonary tumors in mice. I. The susceptibility of the lungs of albino mice to the carcinogenic action of 1,2,5,6-dibenz-anthracene. Pub Health Rep 52: 212-221, 1937. [SGR 5; Cited P242]

3746 Andervont HB: Pulmonary tumors in mice. II. The influence of heredity upon lung tumors induced by the subcutaneous injection of a lard-dibenzanthracene solution. Pub Health Rep 52: 304-315, 1937.

3747 Andervont HB: Pulmonary tumors in mice. III. The serial transmission of induced lung tumors. Pub Health Rep 52: 347-355, 1937.

2062855440

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3748 Andervont HB: Dibenzanthracene tumors in mice. The production of subcutaneous, pulmonary, and liver tumors by serum dispersions and lard solutions. Pub Health Rep 52: 637-647, 1937.

3749 Andervont HB: Dibenzanthracene tumors in mice. The production of subcutaneous and pulmonary tumors by 1,2,5,6-dibenzanthracene adsorbed on charcoal. Pub Health Rep 52: 1931-1940, 1937.

3750 Schnurer L, Haythorn SR: The effects of coal smoke of known composition on rabbit lungs. Am J Pathol 13: 676, 1937.

3751 Hawes JB: Dangerous dusts. N Engl J Med 216: 162-165, 1937.

3752 Auerbach O: Pathology of the pneumoconioses. Ind Med 6: 38-48, 1937.

3753 Teleky L: Occupational cancer of the lung. J Ind Hyg 19: 73-85, 1937. [Cited P281]

3754 Bogen E: Tobacco and tuberculosis. Dis Chest 3: 22; 24, 1937. [SOA 27, Key P27]

3755 Straub M: The microscopical changes in the lungs of mice infected with influenza virus. J Pathol Bacteriol 45: 75-78, 1937. [WHM 247]

3756 Peller S: Further studies on the role of irritation in cancer. Human Biol 9: 57-64, 1937.

3757 Fallon JT: Specific tissue reaction to phospholipids: a suggested explanation for the similarity of the lesions of silcosis and pulmonary tuberculosis. Can Med Assoc J 36: 223-228, 1937.

3758 Cummins SL: Sericite and silica: experimental dust-lesions in rabbits. Br J Exp Pathol 18: 895-401, 1937.

3759 Matz PB: Pathology of the lungs and other organs in silicosis. Milit Surg 81: 88-117, 1937.

3760 Stekol JA, Mann FC: Studies on the mercapturic acid synthesis in animals. II. The role on bile in the absorption and detoxication of bromobenzene and naphthalene in the dog. J Biol Chem 117: 619-627, 1937.

3761 Berenblum I, Bonser GM: Experimental investigation of analine cancer. J Ind Hyg Toxicol 19: 86-92, 1937.

3762 Mottram JC: Production of epithelial tumours by irradiation of a pre-cancerous skin lesion. Am J Cancer 30: 746-748, 1937

3763 Alexander AJP: Carcinoma of bronchus in a boy of 19. Br Med J 2: 116, 1937. [Cited P39]

2062855441

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3764 Behounek F, Sikl FB, Tomicek O: Further research on cancer of the lung in the miners of Jachymov (Joachimstal). Comm Int Congr Sc Campaign Cancer, 2nd Congr, 109-111, 1937.

1938 Monographs and Reviews

3801 Hruby AJ: Chapter 43. Primary carcinoma of the lung. In: Practitioners Library of Medicine and Surgery. New York: Appleton-Century Co., 370-384, 1938.

3802 Klotz MO: Primary carcinoma of the lung. Am J Med Sc 196: 436-454, 1938.

3803+ Filippi J de: El cancer del pulmon. 293 pages. Buenos Aires: El Ateneo, 293 pp, 1938.

3804+ Roume H: Contribution a l'etude du cancer primitif du poumon. Marseille: Leconte, 1-131, 1938.

3805 Dublin LI, Lotka AJ: The mortality from cancer. A study of the mortality experience among the industrial policy holders of the Metropolitan Life Insurance Company 1911-1935. Metrop Life Ins Co Publ, 165-225, 553-561, 1938.

3806 Lanza AJ: Silicosis and asbestosis London: Oxford Univ Press, 1-431, 1938.

1938 Periodicals

3811 Turner HM, Grace HG: An investigation into cancer mortality among males in certain Sheffield trades. J Hyg London 38: 90-103, 1938. [Cited P39, P163]

3812 Boyd W: Some reasons for the recent increase of bronchial carcinoma. Trans Stud Coll Phys Philadelphia 6: 317-328, 1938.

3813 Adams WE: Pneumonectomy for bronchogenic carcinoma of the lung. Report of a successful case 16 months after operation. Ill Med J 74: 442-447, 1938. [Cited P181]

3814 Strode JE, Fennel EA, Burgess CM: Pneumonectomy for carcinoma of the lung with report of a case. Proc Clinic Honolulu 4: 1-10,1938.

3815 Stein JJ, Joslin HL: Carcinoma of the bronchus. A clinical and pathological study of 164 cases. Surg Gynec Obst 66: 902-911, 1938. [Cited P163, P181]

3816 Volini IF, Shapiro WW: Primary carcinoma of the lung. Med Clin NA 20: 123-137, 1938.

2062855442

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3817 Anon: Silicosis and pulmonary carcinoma. Br Med J 2: 411-412, 1938.

3818 Stein JJ: Apical lung tumors. Further observations with report of seven additional cases. JAMA 111: 1612-1617, 1938.

3819 Welker JE, Leger LH: Generalized nodular tuberculosis. Report of a case associated with primary carcinoma of the lung. Am Rev Tuberc 37: 354- 360, 1938.

3820 Carman WL: Malignant tumor involving the lungs: three cases. Med Bull Vet Adm 15: 84-91, 1938.

3821 Overholt RH: Pneumonectomy for malignant and suppurative disease of the lung. Trans N Engl Surg Soc 21: 205-227, 1938.

3822 Overholt RH: Clinical studies and treatment of primary carcinoma of the lung. J Connecticut Med Soc 2: 122-126, 1938. [Cited P180, P181]

3823 King DS: Primary cancer of the lung. N Engl J Med 219: 828-833, 1938. [Cited P181; DMA 530]

3824 Simons EJ: Primary carcinoma of the lungs. Lancet 58: 501-511, 1938. [Cited P181]

3825 McGavack TH: Clinical features of carcinoma of the lung from an analysis of 90 cases. Bull NY Med Coll 1: 129-141, 1938.

3826 Koletsky S: Primary carcinoma of the lung. A clinical and pathologic study of one hundred cases. Arch Int Med 62: 363-651, 1938. [Cited P181, P214]

3827 Matson RC, Roberts JM, Bisaillon M: Total removal of the right lung for bronchogenic carcinoma. Dis Chest 4: 43-46, 1938. [Cited P180, P181]

3828 Anon: Pneumoconiosis and pulmonary carcinoma. JAMA 110: 2086, 1938.

3829 Flick JB, Bauer JT: Primary carcinoma of the lung. Penn Med J 42: 873-876, 1938.

3830 Bauer JT: A review of the primary carcinomas of the lungs and pleurae occurring in six thousand consecutive necropsies. Bull Ayer Clin Lab 3: 139-188, 1938.

3831 Warmolts IJ: Carcinoma of the lung. US Nav Med Bull 36: 79-89, 1938.

3832 Anderson CS, Dible JH: Silicosis and carcinoma of the lung. J Hyg London 38: 185-204, 1938. [Cited P132, P181]

3833 Faget GH, Harmos O: Primary carcinoma of the lung. Report of five cases at U.S. Marine Hospital, Norfolk, Virginia. Virginia Med Month 65: 18-24, 1938.

2062855443

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3834 Vinson PP: The challenge of carcinoma of the lung. Bull Sch Med Univ Maryland 23: 19-21, 1938.

3835 Turner EK, Willis RA: Paraplegia due to metastasis from symptomless, almost invisible bronchial carcinoma. Med J Australia 2: 866-867, 1938. [Cited P290]

3836 Shaw J: Carcinoma of the lug. R Melbourne Hosp Clin Rep 9, 79-82, 1938.

3837 Westermark N: On the roentgen diagnosis of primary tumours of the lung. Acta Radiol 19: 505-527, 1938. [Cited P181]

3838 Edwards AT: Tumours of the lung. Br J Surg 26: 166-192, 1938. [Cited 181]

3839 Allison PR, Stanbury WS: Carcinoma of the lung. Lancet 2: 1165-1167, 1938. [Cited P181]

3840 Barrett NR: Examination of the sputum for malignant cells and particles of malignant growth. J Thorac Surg 8: 169-183, 1938. [Cited P181, P379]

3841 Brock RC: Pulmonary new growths. Pathology, diagnosis, and treatment. Lancet 2: 1103-1108, 1938. [Cited P181]

3842 Owen D, Hewer TF, Whitaker PH: Apical bronchogenic carcinoma. Br Med J 2: 1360-1365, 1938.

3843 Pilcher R: Cancer of the lung. Clin J London 67: 490-493, 1938.

3844 Pilcher R: Cancer of the Lung. Lancet 2: 1131, 1938.

3845 MacDonald EJ: Accuracy of the cancer death records. Am J Pub Health 28: 818-824, 1938. [Cited P208]

3846 Arkin A: A clinical study of 160 cases in five years. J Kansas Med Soc 39: 369-372, 1938. [DMA 542]

3847+ Roffo AH: Unidad cancerigena de los aluitranes des diversos tipos de tabacos. Bol Inst Med Exp 14: 349-406, 1938. [SOA 232, Key P223; DTH Exhibit 64, 65 page 474; TOP 2048; French translation 3947]

3848+ Roffo AH: El tabaco rubio como cancerigeno. Bol Inst Med Exp 15: 5-22, 1938. [SOA 230; DTH Exhibit 62, 63 page 496; TOP 2048; Cited P81, P234]

3849 McCormick WJ: Some medical aspects of tobacco. Can Med Assoc J 38: 67-71, 1938. [Key P384; ERR 50]

2062855444

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3850 Hueper WC, Wiley FH, Wolfe HD: Experimental production of bladder tumors in dogs by administration of beta-naphthylamine. J Ind Hyg 20: 46-84, 1938.

3851 Hueper WC, Briggs FA, Wolfe HD: Experimental investigation of the etiology of aniline tumors. J Ind Hyg Toxicol 20: 85-91, 1938.

3852 Hueper WC: "Aniline tumors" of the bladder. Arch Pathol 25: 856-899, 1938.

3853* Wiley FH, Hueper WC, Bergen DS, Blood FR: The formation of oxalic acid from ethylene glycol and related solvents. J Ind Hyg Toxicol 20: 269-277, 1938.

3854 Greene HSN: Heterologous transplantation of human and other mammalian tumors. Science 88: 357-358, 1938. [Cited P90]

3855 Frank LW: Primary carcinoma of the lung. Rocky Mountain Med J 35: 468-473, 1938.

3856 Matz PB: The incidence of primary bronchiogenic carcinoma. JAMA 111: 2086-2092, 1938. [DMA 539; Cited P181]

3857 Campbell JA: Cancer of the lung. Br Med J 1: 755, 1938.

3858* Kreyberg L: Evidence of extrinsic factors on the development of induced tumours in animals. Acta Pathol Microbiol Scand 37: 317-338, 1938. [Cited in Harris' 1987 article]

3859 Mottram JC: Production of epithelial tumours by a combination of beta radiation and painting with benzpyrene. Am J Cancer 32: 76-79, 1938. [WHM 467]

3860 Anon: Progress of lung cancer experiments. Ann Rep Br Empire Cancer Campaign 15: 148-149, 1938.

3861 Seelig MG, Benignus EL: The production of experimental cancer of the lung in mice. Am J Cancer 33: 519-554, 1938.

3862 Seelig MG, Benignus EL: Lung tumor development in a resistant strain of mice subjected to inhalation of soot. Am J Cancer 34: 391-398, 1938. [Cited P39, P158, P165]

3863 Andervont HB: The incidence of induced subcutaneous and pulmonary tumors and spontaneous mammary tumors in hybrid mice. Pub Health Rep 53: 1665-1671, 1938.

3864 Bittner JJ: Spontaneous lung carcinoma in mice. Pub Health Rep 53: 2197-2202, 1938.

2062855445

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3865 Rous P, Kidd JG: The carcinogenic effect of a papilloma virus on the tarred skin of rabbits. I. Description of the phenomenon. J Exp Med 67: 399-425, 1938. [Cited in Harris' 1987 article]

3866 Little CC: Human heredity and cancer. Bull Am Soc Control Cancer 20: 6, 1938. [ERR 24]

3867 Teleky L: Der Berufliche Lugenkrebs. Acta Union Int Contra Cancrum 3: 253-275, 1938.

3868 Teleky L: Clinical considerations on the question of industrial cancer of asbestos workers. J Ind Hyg Toxicol 20: 184, 1938.

3869 Vorwald AJ, Karr JW: Pneumoconiosis and pulmonary carcinoma. Am J Pathol 14: 49-59, 1938. [Cited P181]

1939 Monographs and Reviews

3901 Behan RJ: Relation of trauma to new growths. Medico-legal aspects. Baltimore: Williams & Wilkins Co., 1-343, 1939.

1939 Periodicals

3911 Anon: Cancer of the lung a growing health problem. Metrop Life Ins Co. Stat Bull 20 (Nov.): 7-9, 1939. [ERR 51; DMA 522; Cited P132]

3912 Anon: Geographic distribution of the decline in mortality from tubercuosis. Metrop Life Ins Co Stat Bull 20 (Mar): 6-9, 1939.

3913 Dolley FS, Jones JC: Surgical treatment of tumors of lung and mediastinum. Am Rev Tuberc 39: 479-487, 1939. [Cited P181]

3914 Holman E, Pierson P: Carcinoma of the lung simulating inflammatory disease. JAMA 113: 108-111, 1939.

3915 Harper FR: Bronchiogenic carcinoma of more than five years' duration treated by radiotherapy. J Thorac Surg 8: 683-688, 1939.

3916 Strode JE, Fennel EA, Burgess CM: Pneumonectomy for carcinoma of the lung. Am J Surg 44: 364-372, 1939. [Cited P181]

3917 Leik DW: Carcinoma of the lung. A case which might have been mistaken for endothelioma of the pleura. J Iowa Med Soc 29: 210-212, 1939.

3918 Jenkinson EL, Hunter AF: Bronchiogenic carcinoma. A diagnostic enigma. JAMA 113: 2392-2398, 1939. [DMA 543]

3919 D'Aunoy R, Pearson B, Halpert B: Carcinoma of the lung. An analysis of seventy-four autopsies. Am J Pathol 15: 567-578, 1939. [Cited P181]

2062855446

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3920 Halpert B: Pathologic aspects of bronchiogenic carcinoma. New Orleans Med Surg J 91: 439-441, 1939. [Cited P181]

3921 Overholt RH, Rumel WR: Clinical studies of primary carcinoma of the lung. An analysis of 70 cases, 20 of which were treated by pneumonectomy or lobectomy. Lancet 59: 155-161, 1939. [DMA 531; Cited P181]

3922 Overholt RH: Apparent cure of primary carcinoma of the lung by pneumonectomy. JAMA 113: 673-674, 1939.

3923 Overholt RH: Pneumonectomy for malignant and supprative disease of the lung. J Thorac Surg 9: 17-61, 1939. [DMA 559]

3924 Craig WM, Woltman HW, Kernohan JW: Metastasis to the central nervous system from carcinoma of the lung. Am J Cancer 36: 12-24, 1939.

3925 Graham EA: Carcinoma of the lung. Proc Interst Postgrad Med Ass NA 400-405, 1939.

3926 Lockwood IH: Primary carcinoma of the bronchus. South Med J 32: 30-34, 1939. [Cited P163]

3927 Pettingill OS: Carcinoma of the lung. Trans Nat Tuberc Assoc NY 35: 145-146, 1939.

3928 Craver LF, Binkley JS: Aspiration biopsy of tumors of the lung. J Thorac Surg 8: 436-463, 1939. [Cited P181, P334]

3929 Hochberg LA, Lederer M: Early manifestations of primary carcinoma of the lung. Arch Int Med 63: 80-99, 1939. [DMA 537; Cited P181]

3930 Howes WE, Schenck SG: Bronchogenic carcinoma. A study of eight autopsied cases. Radiology 32: 8-18, 1939. [DMA 538; Cited P163, P181]

3931 Gebauer PW: A bronchoscopic mirror for upper lobe visualization. J Thorac Surg 9: 89-91, 1939. [Cited P181]

3932 Freedlander SO, Wolpaw SE: Chronic inflammatory lesions of the lung simulating bonchiogenic carcinoma. J Thorac Surg 9: 530-543, 1939.

3933 Behrend M, Behrend A: Total peumonectomy. Arch Surg 38: 698-713, 1939. [Cited P181]

3934 Charache H: Bronchogenic carcinoma with subcutaneous metastases. Am J Cancer 37: 431-434, 1939. [DMA 536]

3935 Reinhoff WF Jr: A two-stage operation for total pneumonectomy in the treatment of carcinoma of the lung, demonstrating a new technique for closure of the bronchus. J Thorac Surg 8: 254-271, 1939. [Cited P181]

2062855447

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3936 Dolley FS, Jones JC: Lobectomy and pneumonectomy for lung suppration and malignancy. Lancet 59: 162-168, 1939. [Cited P181, P379]

3937 Jackson C, Chamberlain WE: Correlation of the bronchoscopic and roentgenologic findings in suspected cancer of the lung. Int Congr Campaign Cancer 3, Congr. 181, 1939.

3938 Bonne C: Morphological resemblance of pulmonary adenomatosis (Jaagsiekte) in sheep and certain cases of cancer of the lung in man. Am J Cancer 35: 491-501, 1939. [Cited P334]

3939+ Thys F: Etiologie du carcinome bronchique. Rev Belge Tuberc 30: 203-204, 1939.

3940+ Roffo AH: El alquitran de cafe cancerigeno. Bol Inst Med Exp 15: 741-762, 1939.

3941+ Roffo AH: Le goudron de cafe cancerigene. Bull Assoc fr cancer 28: 910-924, 1939.

3942* Roffo AH: 1:2-benzopirene. Cancerigeno extraido delalquitran del tobacco. Bol Inst Med Exp 16 1-38, 1939. [SOA 234, Key P237 in German; Cited P81, TOP 2048]

3943 Roffo AH: Sobre los filtros en el tabaquismo. El narguile y el algodon como filtro del alquitran de tobacco. Bol Inst Med Exp 16: 255-268, 1939. [SOA 237; DTH Exhibit 68, 69 page 508; TOP 2048; Cited P81]

3944 Roffo AH: Krebserzeugende Einheit der verschiedenen Tabakteere. Dtsch Med Wochenschr 65: 963-967, 1939. [SOA 235; Key P237; Cited P81]

3945 Roffo AH: Unidad cancerigena de los alquitranes de diversos tipos de tabacos. Bol Inst Med Exp 14: 349-405, 1939. [DMA 426]

3946 Roffo AH: Unidad cancerigena de los alquitranes de diversos tipos de tobacos. Prensa Med Argentina 26: 721-737, 1939. [DMA 401]

3947 Roffo AH: Le goudron de tabac cancerigene. Unite cancerigene des gourdrons de divers types de tabac. Acta Unio Int Contra Cancerum 4: 755-763, 1939. [SOA 233; Key P223; Cited P81, P163, P234; translated from Spanish 3847; Top 895]

3948 Roffo AH: Krebserzeugendes Benzpyren gewonnen aus Tabakteer. Z Krebsforsch 49: 588-597, 1939. [SOA 236; DTH Exhibit 66, 67 page 5001; TOP 2048; Cited P81, P158, P242, P244, P291]

3949 Reinhoff WF Jr: Graded pneumonectomy in the treatment of tumors of the lung. Bull Johns Hopkins Hosp 64: 167-392, 1939. [Cited P181]

2062855448

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3950* Hueper WC: Organic lesions produced by polyvinyl alcohol in rats and rabbits. A toxicopathologic investigation of an experimental thesaurosis. Arch Pathol 28: 510-531, 1939.

3951 Lipowitz H: Primary or bronchogenic carcinoma of the lung. Med J Univ West Ontario 10: 9-16, 1939.

3952 Anon, AMA foreign correspondent in France: Tar on roads and lung cancer. JAMA 113: 245, 1939.

3953 Campbell JA: Carcinogenic agents present in the atmosphere and incidence of primary lung tumours in mice. Br J Exp Pathol 20: 122-132, 1939. [SOA 39; Key P31; Cited P81, P291; DTH Exhibit 71 page 521]

3954 Campbell JA: Carcinogenesis of the lung. Lancet 1: 603-604, 1939.

3955 Magnus HA: The experimental production of malignant papillomata of the lung in mice with 1:2:5:6-dibenzanthracene. J Pathol 49: 21-31, 1939.

3956 Shimkin MB: Production of lung tumors in mice by intratracheal administration of carcinogenic hydrocarbons. Am J Cancer 35: 538-542, 1939. [Cited P158; WHM 141]

3957 Andervont HB: The occurrence of spontaneous and induced pulmonary and liver tumors in strain C3H mice. Pub Health Rep 54: 1158-1169, 1939.

3958 Andervont HB: Pulmonary tumors in mice. VIII. The induction of pulmonary tumors in mice strains D, M, C57 brown, and C57 black by 1:2:5:6-dibenzanthracene. Pub Health Rep 54: 1524-1529, 1939. [SGR 4]

3959 Bittner JJ: Breast and lung carcinoma in "A" stock mice. Pub Health Rep 54: 380-392, 1939.

3960 Rous P, Kidd JG: A comparison of virus-induced rabbit tumors with the tumors of unknown cause elicited by tarring. J Exp Med 69: 399-424, 1939. [Cited P81]

3961 Cottini GB, Mazzone GB: The effects of 3:4-benzpyrene of human skin. Am J Cancer 37: 186-195, 1939. [SGR 63]

3962 Peller S: Lung cancer among mine workers in Joachimsthal. Human Biol 11:130-143, 1939. [Cited P181]

3963 Klotz MO: The association of slicosis and carcinoma of the lung. Am J Cancer 35: 38-49, 1939. [Cited P132, P181]

3964 Lynch KM, Smith WA: Pulmonary asbestosis. V. A report of bronchial carcinoma and epithelial metaplasia. Am J Cancer 36: 567-573, 1939. [Cited P181]

2062855449

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

3965 Lovelock JE: Anthra-silicosis and bronchial carcinoma with quiescent tuberculosis. Br Med J 2: 8-11, 1939.

1940 to 1989 Books and Periodicals

4001 Ewing J: Neoplastic diseases. A treatise on tumors. Fourth Edition, Philadelphia: WB Saunders Co. 81-155; 497-534; 872-1119, 1940. [Key P334; Cited P81, P181, P278; TOP 913; ERR 5]

4002 Palacio J, Mazzei ES: Tumores primitivos malignos bronco-pulmonares. Buenos Aires: El Ateneo 401 pp, 1940.

4115* Roffo AH: Universal toxicomania of tobacco. Cancer and tobacco. (source unknown) [DTH Exhibit 49 page 420-428]

4116* Roffo AH: Correlacion del valor cancerigeno del alquitran de tobaco con el de hulla. Prensa Med Argent 28: 1003-1012, 1941. [Cited P88, P165]

4203* Llambes JJ, Farinas PL, Farinas L, Banet V: Carcinoma primitivo del pulmon. Habana: Biblioteca Medicina de Autores Cubanos 507 pp, 1942.

4311* Schairer E, Schoeniger E: Lungenkrebs und Tabakverbruach. Z Krebsforsch 54: 261-269, 1948.

4801* Fried BM: Bronchiogenic carcinoma and adenoma. With a chapter on mediastinal tumors. Baltimore: Williams & Wilkins Co., 306 pp, 1948.

5801* Fried BM: Tumors of the lungs and mediastinum. Philadelphia: Lea & Febiger 467 pp, 1958.

6101* Larson PS, Haag HB, Silvette H: Tobacco. Experimental and clinical studies. A comprehensive account of the world literature. Baltimore: Williams & Wilkins 932 pp, 1961.

6601* Hueper WC: Occupational and environmental cancers of the respiratory system. New York: Springer-Verlag 215pp, 1966.

7201 Rosenkrantz BG: Public Health and the State. Cambridge: Harvard Univ Press 1-5, 160-182, 1972.

8001 Kovar EB: Major health problems in Massachusetts. A handbook for statewide and local policy makers. Boston: Massachusetts Public Health Association 128 pp, 1980.

8401 Dalton C, Wirkkala J, Thomas A: Leading the way. A history of the Massachusetts General Court 1629-1980. Boston: Office of Massachusettes Secretary of State 487 pp, 1984.

8411* PAHO publication PNSP 84-47. Cited in page ix ref 8802.

2062855450

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000

8701* Rabin R, Korma P, Garbo M, Insogna S, et al: Chemical hazards on the job: Your right to know. Boston: Office of Massachusettes Secretary of State 14 pp, 1987.

8702* Anon: The Commonwealth of Massachusetts. Right to Know. Boston: Office of Massachusettes Secretary of State 1987.

8802 Buck C, Llopis A, Najera E, Terris M: The challenge of epidemiology. Issues and Selected Readings. Washington: Pan American Health Organization Scientific Publication No. 505 989 pp, 1988.

8803 Maulitz RC: Transactions & Studies of the College of Physicians of Philadelphia, Bicentennial Issue, Series V, Vol. X - Unnatural causes: the three leading causes of mortality in America. Philadelphia: College of Physicians. 207 pp, 1988.

8804 Murphy RF: Public Health Trails in Massachusetts. A history and guide. Jamaica Plain: Massachusetts Public Health Association 53 pp, 1988.

8813* Wells CK, Feinstein AR: Detection bias in the diagnostic pursuit of lung cancer. Am J Epidemiol 128: 1016-1026, 1988.

8903* Fustinoni O: Indoor Air Quality. Symposium. Buenos Aires: National Academy of Sciences of Buenos Aires, 1989.

2062855451

Source: https://www.industrydocuments.ucsf.edu/docs/mrgl0000